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=> d his ful

FILE 'REGISTRY' ENTERED AT 16:01:59 ON 12 JUL 2004

L14

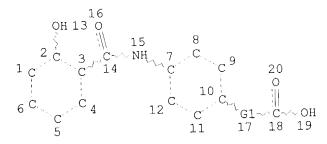
L15 L16

5 SEA SSS SAM L14
57 SEA SSS FUL L14 57 annodes from deg. - see of gove start

FILE 'HCAPLUS' ENTERED AT 16:05:58 ON 12 JUL 2004

33 SEA ABB=ON L16 33 Cets from OA Plus L17

=> d que stat 117 L14



REP G1 = (1-4) C NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE

L16 57 SEA FILE=REGISTRY SSS FUL L14 33 SEA FILE=HCAPLUS ABB=ON L16 L17

=> d ibib abs hitstr 117 1-33

L17 ANSWER 1 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN 2003:696781 HCAPLUS

ACCESSION NUMBER:

139:235382

DOCUMENT NUMBER:

Method for administering GLP-1 molecules orally TITLE:

Khan, Mohammed Amin INVENTOR(S):

Eli Lilly and Company, USA; Jones, Bryan Edward; PATENT ASSIGNEE(S):

McGill, John McNeill PCT Int. Appl., 72 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. KIND | | | | | | DATE APPLICATION NO. DATE | | | | | | | | | | | |
|-----------------|-------------|--------------------------|--------------------------|--------------------------|--------------------------|---|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| WO 2 | | | | Tn - | 1 | 20030 | 1225 | | | | | s311 | | 20030 | | | |
| WO 2 | 20030 W: | AE, CN, FI, KP, | AG, CO, FI, KR, | AL, CR, GB, KZ, | AM, CU, GD, LC, | 20040 AT, CZ, GE, LK, OM, TR, | CZ, GH, LR, | GM, LS, | HR, LT, | HU, LU, | ID, LV, | IL, MA, SC, | IN, MD, SD, | IS, MG, SE, | JP, MK, SG, | KE, MN, SK, | KG, MW, SK, |
| | RW: | ZW, GH, CH, NL, | AM, GM, CY, PT, | AZ, KE, CZ, SE, | BY LS, DE, SI, | MW, DK, SK, | MZ, EE, TR, | SD, ES, BF, | SL, FI, BJ, | SZ, FR, CF, | TZ, GB, CG, | UG, GR, CI, | ZM, HU, CM, | ZW, IE, GA, | AT, IT, GN, | BE, LU, GQ, | BG, MC, |
| ORITY | APP | LN. | INFO | : n.com | กลร | ses f | ormu | lati | US 2 ons | that | 358I | .o4F ionst | rate | the | 0220 fea | sibi | lity |

PRIO

The invention encompasses formulations that demonstrate the feasibilit oral absorption comprising GLP-1 compds. and specified delivery agents. AB

177653-18-8 590383-69-0 RL: BSU (Biological study, unclassified); PEP (Physical, engineering or ITchemical process); PKT (Pharmacokinetics); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (method for administering GLP-1 mols. orally)

177653-18-8 HCAPLUS

Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) RN CN

590383-69-0 HCAPLUS RN

Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]-, monosodium salt (9CI) CN (CA INDEX NAME)

Na

L17 ANSWER 2 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2003:678792 HCAPLUS

DOCUMENT NUMBER:

139:214713

TITLE:

Preparation of novel phenylalanine derivatives as

 $\alpha 4$ integrin inhibitors

Sagi, Kazuyuki; Izawa, Hiroyuki; Chiba, Akira; INVENTOR(S):

Okuzumi, Tatsuya; Yoshimura, Toshiniko; Tanaka, Yuji;

Ono, Miho; Murata, Masahiro Ajinomoto Co., Inc., Japan

PATENT ASSIGNEE(S):

PCT Int. Appl., 163 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. DATE |
|--|--------------------------------|--|---|
| CO, CR, GM, HR, LS, LT, | AL, AM, CU, CZ HU, ID LU, LV | , AT, AU, , DE, DK, , IL, IN, , MA, MD, | WO 2003-JP1852 20030220 AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, |
| RU, TJ, RW: GH, GM, CH, CY, NL, PT, | TM KE, LS CZ, DE SE, SI NE, SN | , MW, MZ, , DK, EE, , SK, TR, , TD, TG | SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, JP 2002-43674 A 20020220 |
| OTHER SOURCE(S): | MA | ARPAT 139: | 214713 |

- * STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY AVAILABLE VIA OFFLINE PRINT *
- The title compds. [I; A = Q, Q1, Q2, Q3; wherein the ring Arm = cycloalkyl or aromatic ring containing 104 heteroatoms selected from O, S, and N; a solid AB line accompanied by a dotted line represents a single or double bond; U, V, X = CO, SO2, CR5R6, C(:CR5R6), C(S), S(O), P(O), P(O)OH, P(O)H; W =CR7, N; R1-R7 = H, halo, HO, lower alkyl, each (un) substituted lower alkyl, lower alkenyl, or lower alkynyl, aryl, heteroaryl, etc.; B = each (un) substituted lower alkoxy, NH2 (excluding NHOH), or SH; C = H, lower

alkyl, lower alkenyl, lower alkynyl, cycloalkyl-lower alkyl (optionally containing a hetero atom in the ring), aryl-lower alkyl, heteroaryl-lower alkyl;D = lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyloxy, cycloalkyl-lower alkyl, or cycloalkyl-lower alkoxy each optionally containing a hetero atom in the cycloalkyl ring, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, etc.; T = CO, C(S), S(O), SO2, NHCO, NHC(S); J, J1 = H, halo, lower alkyl, lower alkoxy, NO2] are prepared These phenylalanine derivs. I have an $\alpha 4$ integrin inhibitory effect and are useful as remedies for various diseases in which $\alpha 4\,$ integrin-dependent adhesion process participates, in particular inflammatory diseases, rheumatoid arthritis, inflammatory bowel diseases, systemic lupus erythematosus, multiple sclerosis, Sjogren syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, or transplant rejection. Thus, (2S)-2-[(2,6-dichlorobenzoyl)amino]-3-[4-[6-(dimethylamino) -1-methyl-2, 4-dioxo-1, 4-tetrahydro-3(2H)quinazolinyl]phenyl]propionic acid (II) (50 mg) (preparation by the solid phase method given), 26 μL Et3N, and 750 νL CH2Cl2 were added to a mixture of 1-chloroethyl cyclohexyl carbonate and 1-iodoethyl cyclohexyl carbonate (420 mg) and stirred at room temperature for 16 h, followed by distillation of

the

solvent and purification by reversed phase HPLC using aqueous acetonitrile containing

0.1% CF3CO2H as the mobile phase to give II 1-[(cyclohexyloxycarbonyl)oxy]ethyl ester trifluoroacetate which is a prodrug of II. II and (2S)-2-[(2-chloro-6-methylbenzoyl)amino]-3-[4-[1methyl-2,4-dioxo-1,4-tetrahydro-3(2H)-quinazolinyl]phenyl]propionic acid inhibited the binding of recombinant human VCAM-1 to human T cell (Jurkat cell) known for expressing integrin $\alpha 4\beta 1$ with IC50 of 57 and 34 nmol/L, resp., and that to human B cell lymphoma cell (RPMI-8866 cell) known for expressing integrin $\alpha 4\beta 7$ with IC50 of 3.3 and 0.2 nmol/L, resp.

401906-04-5DP, Wang resin-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of novel phenylalanine derivs. as $\alpha 4$ integrin inhibitors for treatment of diseases related to α4 integrin-dependent adhesion process)

401906-04-5 HCAPLUS RN

L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-[(2-hydroxybenzoyl)amino]-CN (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L17 ANSWER 3 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
                           2002:695921 HCAPLUS
ACCESSION NUMBER:
                            137:222089
DOCUMENT NUMBER:
                           Compositions for delivery of bisphosphonates
TITLE:
                            Boyd, Maria A. P.; Dinh, Steve
INVENTOR(S):
                           Emisphere Technologies, Inc., USA
PATENT ASSIGNEE(S):
                            PCT Int. Appl., 33 pp.
SOURCE:
                            CODEN: PIXXD2
                            Patent
DOCUMENT TYPE:
                            English
LANGUAGE:
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                   KIND DATE APPLICATION NO. DATE
      PATENT NO.
                                               _____
                        ____
      _____
                                              WO 2002-US6295 20020301
                        A2
                               20020912
      WO 2002070438
      WO 2002070438 AZ 20020912
WO 2002070438 A3 20030424
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
               LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
               PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
               UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                              EP 2002-723294 20020301
                         A2 20040102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 2001-272676P P 20010301
                                             US 2001-272676P P 20010301
WO 2002-US6295 W 20020301
      Compds. and compns. for the delivery of bisphosphonates are provided.
AΒ
      Methods of preparation, administration and treatment are provided as well.
      Typically 400 mg of the delivery agent (sodium N-salicyloyl-8-
      aminocaprylate) was added to 2.0 mL of water. The solution was vortexed,
      then heated (about 37°) and sonicated. The pH was adjusted to
      about 7 with NaOH or HCl. Water was then added to bring the total volume to
      about 2.5 mL. Alendronate (25 \mu L) from a stock solution (made from 2.0 g
      sodium alendronate in 10 mL deionized water, pH adjusted to about 7.5 with
      10 N NaOH, vortexed and sonicated at 37° to obtain a clear solution,
      frozen and defrosted before use) was added to the solution The final doses
      were 200 mg/kg delivery agent compound (i.e., 200 mg delivery agent/kg of
      body weight) and 2.5 mg/kg alendronate, and the volume dose was 1.0 mL/ kg.
      61126-76-9P
 TT
      RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
      BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
      USES (Uses)
```

Benzeneacetic acid, $4-[(2-hydroxybenzoyl)amino]-\alpha-methyl-(9CI)$ (CA

(compns. for delivery of bisphosphonates)

61126-76-9 HCAPLUS

INDEX NAME)

RN

CN

ΙT

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (compns. for delivery of bisphosphonates)

257287-96-0 HCAPLUS

Benzeneacetic acid, $4-[(2-hydroxybenzoyl)amino]-\alpha-methyl-$, RN CN monosodium salt (9CI) (CA INDEX NAME)

● Na

L17 ANSWER 4 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2002:157743 HCAPLUS

DOCUMENT NUMBER:

136:217047

TITLE:

Preparation of novel phenylalanine derivatives having

 $\alpha 4$ integrin-inhibitory activity

INVENTOR(S):

Makino, Shingo; Okuzumi, Tatsuya; Yoshimura, Toshihiko; Satake, Yuko; Suzuki, Nobuyasu; Izawa, Hiroyuki; Sagi, Kazuyuki; Chiba, Akira; Nakanishi,

Eiji; Murata, Masahiro; Tsuji, Takashi

PATENT ASSIGNEE(S):

SOURCE:

Ajinomoto Co., Inc., Japan

PCT Int. Appl., 137 pp. CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND DATE | APPLICATION NO. DATE |
|---|---|--|
| W: AE, AG, CO, CR, GM, HR, LS, LT, | CU, CZ, DE, D HU, ID, IL, I LU, LV, MA, M | 228 WO 2001-JP7039 20010815 AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                                                20010815
                                             AU 2001-78740
                       A5
                             20020304
    AU 2001078740
                                                                20010815
                                             EP 2001-956901
                             20030305
                        Α1
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     EP 1288205
                                                                20010815
                                             JP 2002-521430
                             20030825
                        В2
                                                                20010815
                                             BR 2001-13331
                             20040225
                        Α
     BR 2001013331
                                             US 2002-300856
                                                                20021121
                              20031127
                        A1
     US 2003220268
                                             BG 2003-107555
                                                                20030214
                              20030930
                        Α
     BG 107555
                                             NO 2003-744
                                                                20030217
                              20030407
                        Α
     NO 2003000744
                                                             A 20000818
                                           JP 2000-248728
PRIORITY APPLN. INFO.:
                                                            A 20010517
                                           JP 2001-147451
                                                           W 20010815
                                           WO 2001-JP7039
```

OTHER SOURCE(S):

MARPAT 136:217047

Ι

Phenylalanine derivs. [I; A = Q, Q1, Q2, Q3; wherein Arm = cyclic alkyl or aromatic ring containing 1-4 heteroatom(s) selected from 0, \hat{S} , and N; \hat{U} , \hat{V} , \hat{X} = AΒ CO, SO2, CR5R6, C(:CR5R6), C:S, S:O, P(O)OH, P(O)H; W = CR7, N; wherein R1 - R7 = H, H, halo, OH, (un) substituted lower alkyl, alkenyl, or alkynyl, cycloalkyl optionally containing a heteroatom in the ring, aryl, heteroaryl, etc.; B = HO, lower alkoxy, hydroxyamino; C = H, lower alkyl, alkenyl, alkynyl, cycloalkyl-lower alkyl (optionally containing an heteroatom in the ring), aryl-lower alkyl, heteroaryl-lower alkyl; D = lower alkyl, alkenyl, alkynyl, cycloalkyl or cycloalkyl-lower alkyl (optionally containing an heteroatom in the ring), aryl, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, cycloalkyl-lower alkoxy (optionally containing a heteroatom in the ring), aryloxy, heteroaryloxy, etc.; or C and D are linked to each other to form a ring optionally containing 1 or 2 O, N, or S atom(s); T = CO, C:S, SO, SO2, NHCO, NHCS; J, J' = H, halo, lower alkyl, lower alkoxy, NO2] are prepared by the solid phase method using Wang resin. These compds. are useful for the treatment or prevention of inflammatory disease states related to the $\alpha4$ integrin-dependent adhesion process, e.g. rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, multiple sclerosis, Sjoegren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, atherosclerosis, restenosis, tumor proliferation, tumor metastasis, and transplant rejection. Thus, a solution of Fmoc-Phe(4-NO2)-OH, 2,6-dichlorobenzoyl chloride, and pyridine in N-methylpyrrolidone was added to Wang resin and stirred at room temperature for 16 h to give Fmoc-Phe(4-NO2)-Wang resin which was deprotected by 20% piperidine in DMF at room temperature for 15 min to afford H-Phe(4-NO2)-Wang resin and then acylated by 2,6-dichlorobenzoyl chloride and 2,6-lutidine in N-methylpyrrolidone at room temperature for 16 h to give

2,6-dichlorobenzoyl- Phe(4-NO2)-Wang resin. The latter compound-bound resin was reduced by

SnCl2.2H2O in EtOH/N-methylpyrrolidone at room temperature for 16 h to 2,6-dichlorobenzoyl-Phe(4-NH2)-Wang resin which was cyclocondensed with Me 2-isocyanatobenzoate in N-methylpyrrolidone at room temperature for 16 h to

give

2,6-dichlorobenzoyl-Phe(4-Q)-Wang resin (Q = 1,2,3,4-tetrahydro quinazolin-3-yl) and then methylated by Me iodide in the presence of 18-crown-6 ether and K2CO3 in N-methylpyrrolidone at room temperature for 3

days

to give 2,6-dichlorobenzoyl-Phe(4-Q)-Wang resin (Q = 1-methyl-1,2,3,4-tetrahydroquinazolin-3-yl). Resin-cleavage reaction with 5% aqueous CF3CO2H at room temperature for 1 h gave 2,6-dichlorobenzoyl-Phe(4-Q)-OH (Q = 1-methyl-1,2,3,4-tetrahydroquinazolin-3-yl) (II). II and 2-chloro-6-methylbenzoyl-Phe(4-Q)-OH (Q = 1-methyl-1,2,3,4-tetrahydroquinazolin-3-yl) inhibited the binding of human recombinant VCAM-1 to human T cell Jurikat (ATCC TIB-152) cell expressing integrin $\alpha 4\beta 1$ with IC50 of 1.0 and 0.2 nM, resp.

IT **401906-04-5DP**, Wang resin-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (rejection of)

RN 401906-04-5 HCAPLUS

CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-[(2-hydroxybenzoyl)amino](9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

5

ACCESSION NUMBER:

2001:549162 HCAPLUS

DOCUMENT NUMBER:

136:107380

TITLE:

Oral delivery of biologically active parathyroid

AUTHOR(S):

hormone

Leone-Bay, Andrea; Sato, Masahiko; Paton, Duncan; Hunt, Ann H.; Sarubbi, Donald; Carozza, Monica; Chou,

CORPORATE SOURCE:

Emisphere Technologies, Inc., Tarrytown, NY, 10591,

USA

SOURCE:

Pharmaceutical Research (2001), 18(7), 964-970

James; McDonough, James; Baughman, Robert A.

CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER:
DOCUMENT TYPE:

Kluwer Academic/Plenum Publishers Journal

LANGUAGE:

English

GI

Parathyroid hormone (PTH), the only drug known to stimulate bone AB formation, is a peptide therapeutic indicated in the treatment of osteoporosis. Unfortunately, PTH is only effective when dosed by injection because it has no oral bioavailability. Herein we report the oral absorption of PTH in rats and monkeys facilitated by the novel delivery agent, N-[8-(2-hydroxy-4-methoxy)bensoyl]aminocaprylic acid (I). I was selected from a group of 100 delivery agents based on in vitro chromatog, studies and in vivo screening studies in rats. The PTH/I combination was then tested in monkeys. The interaction of I and PTH was evaluated by NMR spectroscopy. Monkeys were administered an aqueous solution containing \tilde{I} and $\tilde{P}TH$ and mean peak serum PTH concns. of about 3000 pg/mL were obtained. The relative bioavailability of oral PTH was 2.1% relative to s.c. administration. The biol. activity of the orally-delivered PTH was further evaluated in a rat model of osteoporosis. These studies showed that the bone formed following oral PTH/I administration was comparable to that formed following PTH injections. The I mediated absorption of PTH is hypothesized to be the result of a noncovalent interaction between I and PTH. The preliminary evaluation of this interaction by NMR is described. I facilitates the absorption of PTH following oral administration to both The orally-absorbed PTH is biol. active as demonstrated rats and monkeys. in a rat model of osteoporosis.

257951-32-9 345270-28-2 345270-31-7 345270-32-8 345270-34-0 389078-59-5 389078-60-8

RL: PKT (Pharmacokinetics); BIOL (Biological study) (oral delivery of biol. active parathyroid hormone) 257951-32-9 HCAPLUS

Ι

RN 257951-32-9 HCAPLUS
CN Benzenepropanoic acid, 4-[(3-chloro-5-fluoro-2-hydroxybenzoyl)amino](9CI) (CA INDEX NAME)

RN 345270-28-2 HCAPLUS CN Benzenepropanoic acid, 3-fluoro-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 345270-31-7 HCAPLUS CN Benzenepropanoic acid, 4-[(2-hydroxy-5-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \mathsf{OMe} \\ \mathsf{Ho_2C-CH_2-CH_2} \\ & \mathsf{O} \\ & \mathsf{NH-C} \\ \end{array}$$

RN 345270-34-0 HCAPLUS CN Benzenepropanoic acid, 4-[(2-hydroxy-4-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)

$${\rm HO_2C-CH_2-CH_2}$$
 OMe ${\rm NH-C}$

RN 389078-59-5 HCAPLUS CN Benzenepropanoic acid, 4-[(5-fluoro-2-hydroxy-3-methylbenzoyl)amino]-(9CI) (CA INDEX NAME)

RN 389078-60-8 HCAPLUS
CN Benzenepropanoic acid, 3-chloro-4-[(2-hydroxy-4-methoxybenzoyl)amino](9CI) (CA INDEX NAME)

REFERENCE COUNT:

27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2001:453027 HCAPLUS

DOCUMENT NUMBER:

135:45996

TITLE:

Preparation of ω -benzoylaminoalkanoic acids as

drug delivery agents

INVENTOR(S):

Gschneidner, David; Leone-Bay, Andrea; Wang, Eric; Freeman, John J., Jr.; O'Toole, Doris; Shields, Lynn

Ε.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 50 pp. CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

| PATENT NO. KIND DATE | | | | | | | | | APPLICATION NO. DATE | | | | | | | | |
|--------------------------|------|------|-----|-----|-----|------|-------------------------|-----|----------------------|------|---------------|------|-----|------|------|-----|-----|
| WO | 2001 | 0441 | 99 | А | 1 | 2001 | 0621 | | W | 0 20 | 00 - U | S343 | 29 | 2000 | 1218 | | |
| | W: | ΑE, | AG, | AL, | ΑM, | ΑT, | ΑU, | ΑZ, | BA, | BB, | BG, | BR, | BY, | BZ, | CA, | CH, | CN, |
| | | CR, | CU, | CZ, | DE, | DK, | DM, | EE, | ES, | FI, | GB, | GD, | GE, | HR, | ΗU, | ID, | IL, |
| | | IN, | IS, | JP, | KE, | KG, | ΚP, | KR, | KΖ, | LC, | LK, | LR, | LS, | LT, | LU, | LV, | MA, |
| | | MD, | MG, | MK, | MN, | MW, | MX, | ΜZ, | NO, | NΖ, | PL, | PT, | RO, | RU, | SD, | SE, | SG, |
| | | SI, | SK, | SL, | ТJ, | TM, | TR, | TT, | ΤZ, | UA, | UG, | US, | UZ, | VN, | YU, | ZA, | ZW, |
| | | AM, | ΑZ, | BY, | KG, | KΖ, | MD, | RU, | ТJ, | MT | | | | | | | |
| | RW: | GH, | GM, | ΚE, | LS, | MW, | ΜZ, | SD, | SL, | SZ, | ΤZ, | UG, | ZW, | AT, | ΒE, | CH, | CY, |
| | | DE, | DK, | ES, | FI, | FR, | GB, | GR, | IE, | IT, | LU, | MC, | NL, | PT, | SE, | TR, | BF, |
| | | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GW, | ML, | MR, | NE, | SN, | TD, | ΤG | | |
| EΡ | 1237 | 872 | | Α | 1 | 2002 | 0911 | | E | P 20 | 00-9 | 8651 | 6 | 2000 | 1218 | | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | ΙE, | SI, | LT, | LV, | FI, | RO, | MK, | CY, | AL, | TR | | | | | | |
| JP 2003516971 T2 2003052 | | | | | | 0520 | JP 2001-544689 20001218 | | | | | | | | | | |
| US 2003216589 | | | | | 1 | 2003 | 1120 | | U | S 20 | 02-1 | 6827 | 5 | 2002 | 0715 | | |

US 6693208

B2 20040217

PRIORITY APPLN. INFO.:

US 1999-171213P P 19991216 WO 2000-US34329 W 20001218

AB Title compds. were prepared Thus, 2,5-(HO)(MeO)C6H3CO2H was O-protected and the chlorinated product amidated by 8-aminocaprylic acid to give, after deprotection, 2,5-(HO)(MeO)C6H3CONH(CH2)7CO2H. Data for biol. activity of title compds. were given.

IT 345270-28-2P 345270-29-3P 345270-31-7P 345270-32-8P 345270-34-0P 345270-37-3P 345270-38-4P

RL: MOA (Modifier or additive use); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)

(preparation of ω -benzoylaminoalkanoic acids as drug delivery agents)

RN 345270-28-2 HCAPLUS

CN Benzenepropanoic acid, 3-fluoro-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 345270-29-3 HCAPLUS

CN Benzenepropanoic acid, 3-fluoro-4-[(5-fluoro-2-hydroxy-3-methylbenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 345270-31-7 HCAPLUS

CN Benzenepropanoic acid, 4-[(2-hydroxy-5-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \mathsf{NH-C} & \mathsf{OMe} \\ \mathsf{NH-C} & \mathsf{O} \\ \mathsf{OH} \end{array}$$

RN 345270-32-8 HCAPLUS

CN Benzenebutanoic acid, 4-[(2-hydroxy-5-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 345270-34-0 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxy-4-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 345270-37-3 HCAPLUS
CN Benzenepropanoic acid, 3-fluoro-4-[(2-hydroxybenzoyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)

Na

RN 345270-38-4 HCAPLUS
CN Benzenepropanoic acid, 3-fluoro-4-[(5-fluoro-2-hydroxy-3-methylbenzoyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)

$$HO_2C-CH_2-CH_2$$
 O
 $NH-C$
 HO
 Me

● Na

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

1

ACCESSION NUMBER:

2001:380546 HCAPLUS

DOCUMENT NUMBER:

134:367194

TITLE:

Preparation of novel phenylalanine derivatives as

 $\alpha 4$ -integrin inhibitors

INVENTOR(S):

Tanaka, Yasuhiro; Yoshimura, Toshihiko; Izawa, Hiroyuki; Ejima, Chieko; Kojima, Mitsuhiko; Atake, Yuko; Nakanishi, Eiji; Suzuki, Nobuyasu; Makino,

Shingo; Suzuki, Manabu; Murata, Masahiro

PATENT ASSIGNEE(S):

Ajinomoto Co., Inc., Japan PCT Int. Appl., 155 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese 1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PA | TENT | NO. | | KIND DATE | | | | | A | PPLI | CATI | ON NO | 0. | DATE | | | | |
|---------|-------|------|------|-------------|-----|-------|------|------|------|----------|------|-------|-----|----------|------|-----|-----|--|
| WO | 2001 | 0363 | 76 | A1 20010525 | | | | | W | 0 20 | 00-J | P815: | 2 | 20001120 | | | | |
| | W: | ΑE, | ΑG, | AL, | ΑM, | AT, | ΑU, | ΑZ, | BA, | BB, | BG, | BR, | BY, | ΒZ, | CA, | CH, | CN, | |
| | | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EE, | ES, | FI, | GB, | GD, | GE, | GH, | GM, | HR, | |
| | | HU, | ID, | IL, | IN, | IS, | JP, | KΕ, | KG, | ΚP, | KR, | ΚZ, | LC, | LK, | LR, | LS, | LT, | |
| | | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MΖ, | NO, | NΖ, | PL, | PT, | RO, | RU, | |
| | | SD, | SE, | SG, | SI, | SK, | SL, | ТJ, | TM, | TR, | TT, | ΤZ, | UA, | UG, | US, | UZ, | VN, | |
| | | YU, | ZA, | ZW, | AM, | ΑZ, | BY, | KG, | ΚZ, | MD, | RU, | ТJ, | TM | | | | | |
| | RW: | GH, | GM, | KE, | LS, | MW, | ΜZ, | SD, | SL, | SZ, | TZ, | UG, | ZW, | ΑT, | BE, | CH, | CY, | |
| | | DE, | DK, | ES, | FI, | FR, | GB, | GR, | ΙE, | ΙT, | LU, | MC, | NL, | PT, | SE, | TR, | BF, | |
| | | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GW, | ΜL, | MR, | ΝE, | SN, | TD, | TG | | | |
| AU | 2001 | 0141 | 65 | А | 5 . | 2001 | 0530 | | Α | U 200 | 01-1 | 4165 | | 2000 | 1120 | | | |
| EP | 1233 | 013 | | Α | 1 | 2002 | 0821 | | E | P 20 | 00-9 | 7634 | 7 | 2000 | 1120 | | | |
| | R: | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | MC, | PT, | |
| | | ΙE, | SI, | LT, | LV, | FI, | RO, | MK, | CY, | AL, | TR | | | | | | | |
| US | 2003 | 1490 | 83 | А | 1 | 2003 | 0807 | | U | S 200 | 02-1 | 50061 | 7 | 20020 |)520 | | | |
| PRIORIT | Y APP | LN. | INFO | . : | | | | | JP 1 | 999-: | 3284 | 68 | Α | 1999: | 1118 | | | |
| | | | | | | | | ı | JP 2 | 0.00 - 1 | 1971 | 39 | Α | 20000 | 0629 | | | |
| | | | | | | | | I | WO 2 | 000- | JP81 | 52 | W | 2000 | 1120 | | | |
| OTHER S | OURCE | (S): | | | MAR | PAT . | 134: | 3671 | 94 | | | | | | | | | |

GΙ

Phenylalanine derivs. represented by general formula (I) or AΒ pharmaceutically acceptable salts thereof [wherein X represents an interat. bond, O, OSO2, N-(un) substituted NH, NHCO, NHSO2, NHCONH, or NH(CS)NH, CO; Y and Z represent each CO, SO, or SO2; A represents a

specific substituted Ph group or nitrogen-containing heterocycle such as aromatic-fused pyrimidinedione or pyrimidinone, 2,4- or 2,5imidazolidinedione, or 5-imidazolone; C represents hydrogen, lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally containing heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl; D and E represent each lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally containing heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl, etc. or D and E may be bonded to each other to form a ring optionally containing 1 or 2 O, N, or S in the ring; F and G represent each hydrogen, lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally containing heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl, etc. or F and G may be bonded to each other to form a ring; n is from 0 to 2; K represents OR7, NR7R8, NHNR7R8, SR7, or R7; R7 and R8 represents H, lower alkyl, etc.; and J and J' represent each hydrogen, halogeno, lower alkyl, lower alkoxy, or NO2] are prepared These derivs. and analogs thereof show an $\alpha 4$ integrin inhibitory activity and are usable as remedies for various diseases relating to $\alpha 4$ integrin, such as inflammatory diseases related to $\alpha 4$ integrin-dependent adhesion process, arthritis, inflammatory intestinal diseases, systemic lupus erythematosus, multiple sclerosis, Sjoegren syndrome, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, or transplant rejection. Thus, O-(2,6-dichlorobenzyl)-L-tyrosine bound to Wang resin was allowed to react with diethylmalonic acid, HOAt, 2-dimethylaminoisopropyl chloride hydrochloride (DIC), and N-methyl-2-pyrrolidinone (NMP) at room temperature for 16 h, washed with DMF five times, and condensed with pyrroline using HOAt, DIC, and NMP, followed by oxidation with OsO4 in dioxane at room temperature for 16 and resin-cleavage in aqueous CF3CO2H to give N-[2-[(cis-2,4-dihydroxypyrrolidin-1yl)carbonyl]-2-ethylbutanoyl]-0-(2,6-dichlorobenzyl)-L-tyrosine (II). and N-[2-[(pyrrolidin-1-yl)carbonyl]-2-ethylbutanoyl]-4-(2,6dichlorobenzoylamino)-L-phenylalanine inhibited the binding of human recombinant VCAM-1 to human B lymphoma cell line expressing integrin $\alpha 4\beta 7$ with IC50 of $\leq 0.02~\mu mol/L$.

IT 340717-24-0P 340717-60-4P 340717-61-5P 340717-62-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of novel phenylalanine derivs. as $\alpha 4$ -integrin inhibitors)

RN 340717-24-0 HCAPLUS

CN L-Phenylalanine, N-[[1-[(dimethylamino)carbonyl]cyclopropyl]carbonyl]-4[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 340717-60-4 HCAPLUS

N L-Phenylalanine, 4-[(5-bromo-2-hydroxybenzoyl)amino]-N-[[1-[(dimethylamino)carbonyl]cyclopropyl]carbonyl]- (9CI) (CA INDEX NAME) Absolute stereochemistry.

RN 340717-61-5 HCAPLUS

CN L-Phenylalanine, 4-[(5-chloro-2-hydroxybenzoyl)amino]-N-[[1-[(dimethylamino)carbonyl]cyclopropyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 340717-62-6 HCAPLUS

CN L-Phenylalanine, N-[[1-[(dimethylamino)carbonyl]cyclopropyl]carbonyl]-4- [(5-formyl-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2001:297631 HCAPLUS

DOCUMENT NUMBER:

134:316090

TITLE:

Active agent transport systems

INVENTOR(S):

Milstein, Sam J.; Leone-Bay, Andrea; Sarubbi, Donald

J.; Leipold, Harry

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE: '

U.S., 73 pp., Cont.-in-part of U.S. 6,099,856. CODEN: USXXAM

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

| PATENT | NO. | KIND DAT | TE. | APPLICATION NO. | DATE |
|---|---|--|--|--|--|
| US 6221 US 5443 US 5451 US 5578 US 5792 US 5541 US 5629 US 5693 US 6331 ZA 9408 US 5714 US 6099 US 6344 CA 2304 | 367 841 410 323 728 451 155 020 338 318 342 167 856 213 951 | B1 200 A 199 | 010424 050822 050919 061126 050905 080811 060730 070513 071202 011218 050622 080203 000808 020205 | US 1997-939939 US 1992-920346 US 1993-51019 US 1993-76803 US 1993-168776 US 1994-205511 US 1994-231623 US 1994-315200 US 1994-315200 US 1994-316404 ZA 1994-8342 US 1994-328932 US 1996-763183 US 1997-820694 CA 1998-2304951 | 19970929 19920727 19930422 19930614 19931216 19940302 19940422 19940422 19940929 19940930 19941024 19941025 19961210 19970318 19980929 |
| AU 9895 AU 7356 | 427 AL, AM, DK, EE, KR, KZ, NZ, PL, UG, US, GH, GM, FI, FR, CM, GA, 136 93 | A1 199 AT, AU, A2 ES, FI, GE LC, LK, LF PT, RO, RU UZ, VN, YU KE, LS, MW GB, GR, IE GN, GW, MI A1 199 B2 200 | 990408 3, BA, BB, 3, GD, GE, 4, LS, LT, 5, SD, SE, 7, ZW, AM, 7, SD, SZ, 6, IT, LU, 90423 | WO 1998-US20548 BG, BR, BY, CA, CH HR, HU, ID, IL, IS LU, LV, MD, MG, ME SG, SI, SK, SL, TG AZ, BY, KG, KZ, ME UG, ZW, AT, BE, CH MC, NL, PT, SE, BE SN, TD, TG AU 1998-95136 | 19980929 , CN, CU, CZ, DE, , JP, KE, KG, KP, , MN, MW, MX, NO, , TM, TR, TT, UA, , RU, TJ, TM , CY, DE, DK, ES, , BJ, CF, CG, CI, 19980929 |
| R: JP 2001 AU 7710 AU 7714 US 2001 US 2002 US 2002 US 6663 | AT, BE, IE, FI 517694 24 34 039258 127202 155993 898 198658 | T2 200 B2 200 B2 200 A1 200 A1 200 A1 200 B2 200 A1 200 | E, ES, FR, 11009 40311 40325 11108 20912 21024 31216 31023 | US 2001-760307 US 2001-5511 US 2002-125836 US 2003-443713 US 1992-898909 B2 US 1992-920346 A2 US 1993-51019 B2 US 1993-76803 A2 US 1993-143571 B2 US 1993-168776 A2 US 1994-205511 A2 US 1994-205511 A2 US 1994-231622 A2 US 1994-231623 B2 WO 1994-US4560 A2 US 1994-315200 A2 | 1, NL, SE, MC, PT, 19980929 20001214 20001214 20010111 20011107 20020419 20030521 19920615 19920727 |

US 1994-328932 A2 19941025 US 1996-17902P P 19960329 A2 19961210 US 1996-763183 US 1997-820694 A2 19970318 US 1997-939939 A 19970929 AU 1998-62756 A3 19980206 WO 1998-US20548 W 19980929 US 2001-929530 A1 20010813 US 2002-125836 A1 20020419

Methods for transporting a biol. active agent across a cellular membrane AΒ or a lipid bilayer includes the steps of: (a) providing a biol. active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. active agent to a complexing perturbant to reversibly transform the biol. active agent to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. active agent across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. active agent. In the present invention, the biol. active agent does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. active agent comprising steps (a) and (b) above is also provided as are oral delivery compns. Addnl., mimetics and methods for preparing mimetics are contemplated. One example gives penetrant phenylsulfonyl-p-aminobenzoic acid effect on α -interferon.

IT 183990-74-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (active agent transport systems containing complexing pertubants and biol. agents)

RN 183990-74-1 HCAPLUS

CN Butanedioic acid, [4-[(2-hydroxybenzoyl)amino]phenyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

721 THERE ARE 721 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L17 ANSWER 9 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:492070 HCAPLUS

DOCUMENT NUMBER:

133:109955

TITLE:

Amino acid derivatives and compositions therewith for

delivering active agents

INVENTOR(S):

Leone-Bay, Andrea; Ho, Koc-kan; Sarubbi, Donald J.;

Leipold, Harry R.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 44 pp., Cont.-in-part of PCT 9736480.

CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

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PATENT NO. KIND DATE APPLICATION NO. DATE
                                      ______
    _____ ___
                   A 20000718 US 1997-797816 19970207
A1 19971009 WO 1997-US5128 19970318
    US 6090958 A
    WO 9736480
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
           DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
           LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
           RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
           YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
           GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
           ML, MR, NE, SN, TD, TG
                                      CA 1998-2319672 19980206
    CA 2319672 AA 19980813
                                      CA 1998-2319680 19980206
WO 1998-US2619 19980206
    CA 2319680 AA 19980813
WO 9834632 A1 19980813
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
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           KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
           PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
           ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
           FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
            GA, GN, ML, MR, NE, SN, TD, TG
    AU 9862756 A1 19980826
                                      AU 1998-62756
                                                     19980206
                         20010927
    AU 738735
                    В2
                                      EP 1999-117292 19980206
    EP 993831
                    A2
                         20000419
                    A3 20010502
    EP 993831
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                    A1 20000705 EP 1998-905042 19980206
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                                    EP 2000-122704 19980206
    EP 1093819
EP 1093819
                          20010425
                    A2
                   A3 20030514
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
           IE, FI
                                                      19980206
                                       JP 2000-311231
    JP 2001131090
                    A2
                          20010515
                                       JP 2000-311230 19980206
    JP 2001139494
                          20010522
                   A2
                   T2 20010828
A 20010831
A 20000531
A 20011130
                                                      19980206
                                       JP 1998-535034
    JP 2001513080
    NZ 337131
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                                                      19980206
                                      MX 1999-7290
                                                       19990806
    MX 9907290
                                      NZ 2000-507275
                                                       20001003
    NZ 507275
                                      NZ 2000-507276 20001003
                   A 20020201
    NZ 507276
                  B2 20040311
B2 20040325
                                      AU 2000-72261
                                                        20001214
    AU 771024
                                                       20001214
    AU 771434
                                       AU 2000-72260
PRIORITY APPLN. INFO.:
                                    US 1996-17902P P 19960329
                                                   A2 19970318
                                     WO 1997-US5128
                                                   A1 19960329
                                     US 1996-17902
                                                    A 19970207
                                     US 1997-796334
                                                   A 19970207
                                     US 1997-796335
                                                   A 19970207
                                     US 1997-796336
                                                    A 19970207
                                     US 1997-796337
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A 19970207
US 1997-796338
               A 19970207
US 1997-796339
               A 19970207
US 1997-796340
                A 19970207
US 1997-796341
                A 19970207
US 1997-797100
                A 19970207
US 1997-797813
                A 19970207
US 1997-797816
               A 19970207
US 1997-797817
               A 19970207
US 1997-797820
               A3 19980206
AU 1998-62756
CA 1998-2279331 A3 19980206
               A3 19980206
EP 1998-905042
                A3 19980206
EP 1999-117292
JP 1998-535034
              A3 19980206
               A1 19980206
NZ 1998-337131
WO 1998-US2619
                W 19980206
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AB Carrier compds., especially amino acid derivs., and compns. therewith which are useful in the delivery of active agents, e.g. peptides, mucopolysaccharides, carbohydrates, and lipids, are provided. Methods of administration and preparation are provided as well. An intracolonic dosing composition containing parathyroid hormone 25 μg/kg, 4-[4-(phenoxyacetyl)aminophenyl]butyric acid as carrier 100 mg/kg in 25% aqueous propylene glycol was prepared

209961-45-5P 209961-80-8P 209961-83-1P 209961-85-3P 209962-03-8P 209962-04-9P 209962-15-2P 209962-17-4P 211511-75-0P 211511-91-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino acid derivs. as drug carriers for biol. active components)

RN 209961-45-5 HCAPLUS

CN Benzenebutanoic acid, 4-[[(1-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 209961-80-8 HCAPLUS

CN Benzenebutanoic acid, 4-[(5-chloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 209961-83-1 HCAPLUS

CN Benzenebutanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI)

(CA INDEX NAME)

RN 209961-85-3 HCAPLUS

CN Benzenepropanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 209962-03-8 HCAPLUS

CN Benzenebutanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 209962-04-9 HCAPLUS

CN Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 209962-15-2 HCAPLUS

CN Benzeneacetic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 209962-17-4 HCAPLUS

CN Benzenepentanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 211511-75-0 HCAPLUS

CN Benzenebutanoic acid, 4-[(4-bromo-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 211511-91-0 HCAPLUS

CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]-γ-οxο- (9CI) (CA INDEX NAME)

L17 ANSWER 10 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:475505 HCAPLUS

DOCUMENT NUMBER:

133:109945

TITLE:

Polymeric delivery agents comprising a polymer conjugated to a modified amino acid or derivative

thereof

INVENTOR(S):

Milstein, Sam J.; Barantsevitch, Eugene N.; Wang, Nai Fang; Liao, Jun; Smart, John E.; Conticello, Richard D.; Ottenbrite, Raphael M.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA; Virginia

Commonwealth University PCT Int. Appl., 91 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| | PAC | CENT : | NO. | | KIND DATE | | | | | | ICATI | 0. | DATE | | | | | |
|-------|---------------------|---|------------|------------|---------------------------------|---------------------------------|---------------------------------|--------------------------|-------------------|----------------|----------------------|-------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| | | | | | A2 20000713 A3 20001214 | | | | | | | 20000107 | | | | | | |
| | | W: AE, AL, CZ, DE, JP, KE, MN, MW, TM, TR, KZ, MD, | | | AM, DK, KG, MX, TT, | AT, DM, KP, NO, TZ, | AU, EE, KR, NZ, UA, | AZ, ES, KZ, PL, | FI, LC, PT, | GB LK RO | , GD , LR , RU | , GE, , LS, , SD, | HR, LT, SE, | HU, LU, SG, | ID, LV, SI, | IL, MD, SK, | IN, MG, SL, | IS, MK, TJ, |
| | | RW: | GH, DK, | GM, ES, | KE, FI, | LS, FR, | MW, GB, | GR, | ΙE, | IΤ | , LU | , UG, , MC, , SN, | NL, | PT, | | | | |
| | | 2358 | | | | | | | | | | | | | | | | |
| | EΡ | 1146 | | | | | | | | | | | | | | | | D.M. |
| | | R: | | | | | DK, FI, | | FR, | GB, | , GR | , IT, | ш⊥, | LU, | NĿ, | SE, | MC, | PT, |
| | BR | 2000 | | | | | | | |] | BR 2 | 8-00C | 590 | | 2000 | 0107 | | |
| | JΡ | 2002 | 5343 | 63 | T. | 2 | 2002 | 1015 | | | JP 2 | 000-5 | 9196 | 1 | 2000 | 0107 | | |
| | | 5125 | | | | | | | | | | 000-5 | | | | | | |
| | ZA | ZA 2001005213 | | | | | 2002 | 0717 | | | | 001-5 | | | | | | |
| | US 6627228 | | | | | | | | | | | 001-8 | | | | | | |
| | | | | | | | | | | | | | | 2003 | | | | |
| PRIOF | RIORITY APPLN. INFC | | | | .: | | | | 1 | WO : | 2000- | -1152 -US47 -8890 | 6 | M | 2000 | 0107 | | |

Polymeric delivery agents comprising a polymer conjugated to a modified AΒ amino acid or derivative thereof, delivery agent compds. and compns. comprising them which are useful in the delivery of active agents are provided. Poly(N-acryloxysuccinimide) was conjugated with N-(5-aminomethylsalicyloyl)-8-aminocaprylic acid (preparation given). Oral andintracolonic delivery composition comprising human growth hormone and above conjugate was administered to rats. At a dose of 200 mg/kg conjugate, the actual amount of delivery agent dosed was 20 mg/kg. With such a concentration

delivery agent complexed with polymer there was evidence of systemic delivery.

177653-18-8P 283599-46-2P ΙT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(polymeric delivery agents comprising polymer conjugated to modified amino acid or derivative thereof)

RN 177653-18-8 HCAPLUS

of

Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

RN 283599-46-2 HCAPLUS

CN Benzenebutanoic acid, 4-[[5-(aminomethyl)-2-hydroxybenzoyl]amino]- (9CI) (CA INDEX NAME)

L17 ANSWER 11 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: DOCUMENT NUMBER:

2000:117018 HCAPLUS 132:151567

TITLE:

Preparation of arylamidoalkylcarboxylic acids and

compositions for delivering active agents.

INVENTOR(S):

Gschneidner, David; Leone-Bay, Andrea; Wang, Eric; Errigo, Lynn; Kraft, Kelly; Moye-Sherman, Destardi; Ho, Koc-Kan; Press, Jeffrey Bruce; Wang, Nai Fang

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA PCT Int. Appl., 53 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PAI | | NO. | | | | DATE | | | A | PPLI(| CATI | N NC | o. | DATE | | | | | |
|-----|---------------------|------|-----|-----|-------------|------|------|-----|-----|-------|------|------|-----|------|------|-----|-----|--|--|
| | 2000 | 0079 | 79 | A | A2 20000217 | | | | W | 0806 | | | | | | | | | |
| WO | 2000 | | | | | | | | | | | | | | | | | | |
| | W: | ΑE, | AL, | ΑM, | ΑT, | ΑU, | ΑZ, | ΒA, | BB, | BG, | BR, | ΒY, | CA, | CH, | CN, | CR, | CU, | | |
| | | CZ, | DE, | DK, | EE, | ES, | FΙ, | GB, | GD, | GE, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | | |
| | | KE, | KG, | KP, | KR, | ΚZ, | LC, | LK, | LR, | LS, | LT, | LU, | LV, | MD, | MG, | MK, | MN, | | |
| | | | | | | PL, | | | | | | | | | | | | | |
| | | | | | | US, | | | | | | | | | | | | | |
| | | RU, | TJ, | TM | | | | | | | | | | | | | | | |
| | RW: | GH, | GM, | ΚE, | LS, | MW, | SD, | SL, | SZ, | UG, | ZW, | AT, | BE, | CH, | CY, | DE, | DK, | | |
| | | | | | | GR, | | | | | | | | | | | | | |
| | | CI, | CM, | GΑ, | GN, | GW, | ML, | MR, | NE, | SN, | TD, | TG | | | | | | | |
| CA | 2339 | | | | | | | | | | | | 65 | 1999 | 0806 | | | | |
| ΑU | 9954 | 711 | | Α | 1 | 2000 | 0228 | | A | U 19 | 99-5 | 4711 | | 1999 | 0806 | | | | |
| EΡ | 1102742 A2 20010530 | | | | | | | | Ε | P 19 | 99-9 | 4096 | 7 | 1999 | 0806 | | | | |
| | | | | | | DK, | | | | | | | | | | | PT, | | |
| | | | | | | FI, | | | | | | | | | | | | | |
| BR | 9912 | | | | | | | | В | R 19 | 99-1 | 2975 | | 1999 | 0806 | | | | |

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TR 2001-20010036619990806
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     TR 200100366
                       Т2
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                                                            19990806
                                          NZ 1999-509410
                            20030829
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                       Α
                                                            20010117
                                           ZA 2001-470
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                                                         Ρ
                                                            19980807
PRIORITY APPLN. INFO .:
                                                         Р
                                                            19980831
                                        ÚS 1998-98500P
                                        US 1998-108366P P
                                                            19981113
                                        US 1999-119207P P
                                                            19990205
                                        WO 1999-US17974 W 19990806
     135 Title compds. are claimed. Thus, Me azeloyl chloride was added
AΒ
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AB 135 Title compds. are claimed. Thus, Me azeloyl chloride was added dropwise to 2-amino-p-cresol in aqueous NaOH at 0° to give a residue which was stirred with aqueous NaOH in THF to give 4-HO-5-MeC6H3NHCO(CH2)7CO2H. Title compds. at 100-300 mg/kg with parathyroid hormone at 25-200 μg orally or intracolonically in rats gave peak serum parathyroid hormone levels of 5-1459.71 pg/mL.

1T 257951-31-8P 257951-32-9P 257951-33-0P 257951-34-1P 257951-35-2P 257951-38-5P 257951-39-6P 257951-40-9P 257951-41-0P 257951-44-3P 257951-45-4P 257951-97-6P 257951-98-7P 257952-02-6P 257952-19-5P 257952-40-2P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of arylamidoalkylcarboxylic acids and compns. for delivering active agents)

RN 257951-31-8 HCAPLUS

CN Benzenepropanoic acid, 4-[(5-chloro-3-fluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 257951-32-9 HCAPLUS CN Benzenepropanoic acid, 4-[(3-chloro-5-fluoro-2-hydroxybenzoyl)amino]-(9CI) (CA INDEX NAME)

RN 257951-33-0 HCAPLUS CN Benzenepropanoic acid, 4-[(2-hydroxy-3,5-dimethylbenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 257951-34-1 HCAPLUS CN Benzenebutanoic acid, 4-[(2-hydroxy-3,5-dimethylbenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 257951-35-2 HCAPLUS
CN Benzenepropanoic acid, 4-[(3-bromo-5-chloro-2-hydroxybenzoyl)amino]- (9CI)
(CA INDEX NAME)

RN 257951-38-5 HCAPLUS
CN Benzenepropanoic acid, 4-[(3,5-difluoro-2-hydroxybenzoyl)amino]- (9CI)
(CA INDEX NAME)

RN 257951-39-6 HCAPLUS
CN Benzenebutanoic acid, 4-[(3,5-difluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 257951-40-9 HCAPLUS

CN Benzenepropanoic acid, 4-[(5-fluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 257951-41-0 HCAPLUS

CN Benzenebutanoic acid, 4-[(5-fluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 257951-44-3 HCAPLUS

CN Benzenebutanoic acid, 4-[(5-fluoro-2-hydroxy-3-methylbenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 257951-45-4 HCAPLUS

CN Benzenebutanoic acid, 4-[(5-chloro-2-hydroxy-3-methylbenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 257951-97-6 HCAPLUS

CN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]-3-methyl- (9CI) (CA INDEX NAME)

RN 257951-98-7 HCAPLUS

CN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]-3-methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{O} & \text{CH}_2\text{--}\text{CH}_2\text{--}\text{CO}_2\text{H} \\ \hline \\ \text{OH} & \text{OMe} \\ \end{array}$$

RN 257952-02-6 HCAPLUS

CN Benzenepropanoic acid, 2-fluoro-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 257952-19-5 HCAPLUS

CN Benzenebutanoic acid, 4-[(2-hydroxy-4-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)

257952-40-2 HCAPLUS RN Benzenepropanoic acid, 4-[(5-chloro-2-hydroxy-3-methylbenzoyl)amino]-CN (9CI) (CA INDEX NAME)

L17 ANSWER 12 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:98355 HCAPLUS

DOCUMENT NUMBER:

132:141984

TITLE:

Pulmonary delivery of active agents

INVENTOR(S):

Milstein, Sam J.; Smart, John E.; Sarubbi, Donald J.; Carozza, Monica; Flanders, Elizabeth; O'Toole, Doris;

Leone-Bay, Andrea; Gschneidner, David

PATENT ASSIGNEE(S):

SOURCE:

Emisphere Technologies, Inc., USA

PCT Int. Appl., 47 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

English LANGUAGE: 1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. DATE PATENT NO. KIND DATE _____ ----_____ A1 20000210 WO 2000006184 WO 1999-US16957 19990727 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG CA 1999-2338358 19990727 20000210 CA 2338358 AA CA 2338419 AΑ 20000210 CA 1999-2338419 19990727 WO 1999-US17090 19990727 A1 20000210 WO 2000006534 AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,

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             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                       A1
     AU 9953210
                            20000221
                                           AU 1999-53210
                                                             19990727
     AU 745290
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                       A1
                            20000221
                                           AU 1999-53237
                                                             19990727
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                                            EP 1999-938806
                                                             19990727
     EP 1100522
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                            20010523
                                                             19990727
     EP 1100771
                                            EP 1999-938842
                       A1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     TR 200100922
                            20010921
                                            TR 2001-20010092219990727
                       Т2
     BR 9912694
                       Α
                            20020102
                                            BR 1999-12694
                                                             19990727
     JP 2002521455
                       Т2
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                                                             19990727
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                                           NZ 1999-509239
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                       Α
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                       Т2
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                                            JP 2000-562341
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                       Α
                                                             19990727
     ZA 2001000227
                            20010807
                       Α
                                            ZA 2001-227
                                                             20010109
     ZA 2001000226
                       Α
                            20010904
                                            ZA 2001-226
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                                                             20020614
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                            20031204
                                           US 2003-600413
                                                             20030620
                                                             19980727
                                         US 1998-94267P
PRIORITY APPLN. INFO.:
                                                         Ρ
                                                             19981016
                                        US 1998-104466P P
                                                            19990727
                                        WO 1999-US16957
                                                         W
                                        WO 1999-US17090 W 19990727
                                        US 2001-744862
                                                          A1 20010419
                                         US 2001-744777
                                                          A1 20010426
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OTHER SOURCE(S): MARPAT 132:141984

AB Methods of administration of active agents via the pulmonary route are provided. Thus, sodium 2-(4-(N-salicyloyl)aminophenyl)propionate was prepared and 16 mg/kg this compound was mixed with 0.05 mg/kg porcine insulin and administered to rats by lung-spray-IT instillation. The AUC of the formulation wa higher than that without any carrier added.

IT 61126-76-9P 257287-96-0P

RN 61126-76-9 HCAPLUS

CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- α -methyl- (9CI) (CA INDEX NAME)

RN 257287-96-0 HCAPLUS

CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- α -methyl-, monosodium salt (9CI) (CA INDEX NAME)

Na

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:649906 HCAPLUS

DOCUMENT NUMBER:

132:40404

TITLE:

Transport of human growth hormone across Caco-2 cells

with novel delivery agents: evidence for

P-glycoprotein involvement

AUTHOR(S):

Wu, S.-J.; Robinson, J. R.

CORPORATE SOURCE:

School of Pharmacy, University of Wisconsin, Madison,

WI, USA

SOURCE:

Journal of Controlled Release (1999), 62(1-2), 171-177

CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER:

Elsevier Science Ireland Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Emisphere Technologies, Inc. has synthesized a series of small mols. which have been shown to improve protein absorption through mucosal tissue. This enhancement is specific between protein and a particular delivery agent. Despite the specificity of interaction, the mechanism of enhanced tissue penetration is still unclear. The purpose of this work is to understand the enhancement mechanism(s) of these delivery agents by using Caco-2 cells as a model membrane. It was found that the bidirectional transepithelial fluxes of human growth hormone (hGH) in the presence of these delivery agents across human intestinal epithelial Caco-2 cell line showed marked asymmetry. Average permeability coefficient values obtained in

the

apical (AP) to basolateral (BL) direction were lower than those of the reverse (BL to AP) direction. On the other hand, the fluxes for human growth hormone alone were sym. When P-glycoprotein inhibitors were included in the transport medium, the permeability coefficient values of BL to AP direction were significantly decreased while the transport was increased in the reverse direction in the presence of delivery agents. P-glycoprotein inhibitors had no effect on the transport of human growth hormone alone. This study shows that human growth hormone alone can be transported across Caco-2 cells in very limited quantities by passive diffusion, but in the presence of delivery agents, human growth hormone can be effluxed in a P-glycoprotein-mediated fashion. This also indirectly shows that the human growth hormone has become more lipophilic in the presence of delivery agents.

IT **177653-18-8**, e352

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use);

BIOL (Biological study); PROC (Process); USES (Uses) (transport of human growth hormone across Caco-2 cells with novel delivery agents)

RN 177653-18-8 HCAPLUS

Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

REFERENCE COUNT:

21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:548469 HCAPLUS

DOCUMENT NUMBER:

131:291168

TITLE:

Transcellular and lipophilic complex-enhanced intestinal absorption of human growth hormone

Wu, Sy-Juen; Robinson, Joseph R.

AUTHOR(S): CORPORATE SOURCE:

School of Pharmacy, University of Wisconsin-Madison,

Madison, WI, 53706, USA

SOURCE:

Pharmaceutical Research (1999), 16(8), 1266-1272

CODEN: PHREEB; ISSN: 0724-8741 Kluwer Academic/Plenum Publishers

PUBLISHER:

Journal

DOCUMENT TYPE:

LANGUAGE: English

To evaluate the transcellular mechanism of novel enhancers absorption enhancement of human growth hormone (hGH), by examining the involvement of a P-glycoprotein-like efflux system, changes in membrane fluidity, and membrane damage, Caco-2 cell monolayers were grown on Snapwell filter supports and placed in a side-by-side diffusion apparatus Transport in both the apical to basolateral (AP to BL) and basolateral to apical (BL to AP) direction was measured at different temps, and in the presence of potential inhibitors. Fluorescence anisotropy measurement was used to measure membrane fluidity. The fluorescence anisotropy of DPH- and TMA-DPH-labeled cell suspensions was measured at room temperature LDH (a measure of cytosolic lactate dehydrogenase) leakage assay was used to evaluate cytotoxicity. The bi-directional transepithelial fluxes of hGH in the presence of these novel enhancers across Caco-2 cells showed marked asymmetry. Average permeability coefficient values obtained in the apical to basolateral (AP to BL) direction were lower than those of the reverse (BL to AP) direction. On the other hand, the fluxes for hGH alone were sym. When P-gp-like efflux inhibitors were included in the transport medium, the permeability coefficient value of BL to AP direction was significantly decreased while the transport was increased in the reverse direction in the presence of novel enhancers. In addition, lowering the temperature to 25°C completely eliminated the asymmetry of hGH transport in the presence of novel enhancers. It was also shown by fluorescence anisotropy that these novel enhancers alone only slightly increased membrane fluidity. On the other hand, upon addition of hGH to the novel enhancers, the cell membrane showed a dramatic change as compared to treatment with novel enhancers alone. The results from the LDH assay showed that the novel enhancers and/or hGH did not cause cell damage, at least up to 1 h, and the damage seen at the 2 h point is also much lower than other known enhancers. This study shows that human growth hormone alone cannot be

transported across Caco-2 cells, except in small quantities, by passive diffusion, but in the presence of novel enhancers, human growth hormone permeation is substantial. In addition, the asymmetry of transport of the complexed hGH appears to be due to a P-gp-like efflux system. Assuming that the present substrate specificity of the P-qp-like efflux system shows the same preference for hydrophobic mols. as p-qp, the present work also indirectly shows that human growth hormone has become more lipophilic in the presence of these novel enhancers. Furthermore, membrane fluidity data also supports the premise that these novel enhancers interact and stabilize hGH, to make them more hydrophobic and easier to be transported through cell membranes.

177653-18-8, E352

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(transcellular and lipophilic complex-enhanced intestinal absorption of human growth hormone)

RN 177653-18-8 HCAPLUS

Benzenebutanoic acid, 4-((2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS 23 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 15 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:211174 HCAPLUS

131:23376 DOCUMENT NUMBER:

TITLE:

Barriers and potential solutions to controlled drug

delivery across mucosal tissues

AUTHOR(S):

Robinson, Joseph R.

CORPORATE SOURCE:

School of Pharmacy, University of Wisconsin, Madison,

WI, 53706, USA

SOURCE:

Polymer Preprints (American Chemical Society, Division

of Polymer Chemistry) (1999), 40(1), 254-255

CODEN: ACPPAY; ISSN: 0032-3934

PUBLISHER:

American Chemical Society, Division of Polymer

Chemistry

DOCUMENT TYPE:

Journal

LANGUAGE:

English

The use of enhancers such as a phenylbutyric acid to improve the transport of human growth hormone across Caco-2 cells and mucosal tissues is discussed.

177653-18-8, E352 ΙT

> RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (barriers to controlled drug delivery across mucosal tissues)

RN 177653-18-8 HCAPLUS

Benzenebutanoic acid, 4-[(2-hydroxybenzovl)amino]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 16 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:100747 HCAPLUS

DOCUMENT NUMBER:

130:144204

TITLE:

Modified amino acids as carriers for enhanced delivery

of active agents

INVENTOR(S):

Leone-Bay, Andrea; Ho, Koc-kan; Sarubbi, Donald J.;

Milstein, Sam J.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 414,654.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. DATE |
|---|---|--|--|
| US 5866536 US 5650386 CN 1190893 JP 2003313157 US 6071510 AU 771024 AU 771434 PRIORITY APPLN. INFO.: | A A A A A2 A B2 B2 | 19990202 19970722 19980819 20031106 20000606 20040311 20040325 | US 1997-798033 19970206 US 1995-414654 19950331 CN 1996-192998 19960401 JP 2003-140962 19960401 US 1997-839094 19970423 AU 2000-72261 20001214 AU 2000-72260 20001214 US 1995-414654 A2 19950331 US 1995-3111P P 19950901 JP 1996-529751 A3 19960401 |
| | | 20040325 | US 1995-414654 A2 19950331 US 1995-3111P P 19950901 |

Carrier compds., compns., and dosage unit forms which are useful in the delivery of active agents are provided. The present invention provides compds. such as 10-salicyloylaminodecanoic acid (I) for delivery of at least one active agent, including peptides, mucopolysaccharides, carbohydrates, or lipids. I prepared from 8-aminocaprylic acid and O-acetylsalicyloyl chloride was mixed with recombinant human growth hormone (rhGH) in a phosphate buffer solution. The composition was orally administered to rats at I 200 mg/kg and rhGH 3 mg/kg and delivery was evaluated by an ELISA assay for rhGH; mean peak serum levels of rhGH was .apprx.60.92 ng/mL as compared to <0.1 ng/mL for control group received a composition without I.

IT 183990-74-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (modified amino acids as carriers for enhanced delivery of active agents)

RN 183990-74-1 HCAPLUS

CN Butanedioic acid, [4-[(2-hydroxybenzoyl)amino]phenyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 17 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:27805 HCAPLUS

DOCUMENT NUMBER:

130:95843

TITLE:

Preparation of cyclopentylcarbonylamino acid as

inhibitors of $\alpha 4\beta 1$ mediated cell adhesion

INVENTOR(S):

Lobl, Thomas J.; Rishton, Gil; Teegarden, Bradley; Polinsky, Alex; Yamagishi, Masafumi; Tanis, Steven P.;

Fisher, Jed F.; Thomas, Edward W.; Chrusciel, Robert

PATENT ASSIGNEE(S):

Tanabe Seiyaku Co., Ltd., Japan; Pharmacia & Upjohn

Company

SOURCE:

PCT Int. Appl., 342 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA | TENT | NO. | | KIND DATE | | | | | | | | | DATE | | | | |
|----------|-------|------|------|--------------|-----|-------|-------|-------|------|------|-------|-------|------|-------|------|-----|-----|
| WO | 9858 | | | А | 1 | 1998 | 1230 | | V | 70 1 | | JS130 | 64 | | | | |
| | W: | AL, | AM, | ΑT, | ΑU, | ΑZ, | BA, | BB, | BG, | BR | , BY, | CA, | CH, | CN, | CU, | CZ, | DE, |
| | | DK, | EE, | ES, | FI, | GB, | GE, | GH, | GM, | GW | , HU, | ID, | IL, | IS, | JP, | KE, | KG, |
| | | KΡ, | KR, | KΖ, | LC, | LK, | LR, | LS, | LT, | LU | , LV, | MD, | MG, | MK, | MN, | MW, | MX, |
| | | NO, | NΖ, | PL, | PT, | RO, | RU, | SD, | SE, | . SG | , SI, | SK, | SL, | TJ, | TM, | TR, | TT, |
| | | UA, | UG, | US, | UΖ, | VN, | YU, | ZW, | AM, | AZ | , BY, | KG, | KZ, | MD, | RU, | ТJ, | TM |
| | RW: | GH, | GM, | ΚE, | LS, | MW, | SD, | SZ, | UG, | ZW | , АТ, | BE, | CH, | CY, | DE, | DK, | ES, |
| | | FI, | FR, | GB, | GR, | ΙE, | ΙΤ, | LU, | MC, | NL | , PT, | SE, | BF, | BJ, | CF, | CG, | CI, |
| | | | | | | MR, | | | | | | | | | | - | • |
| | 9881 | | | | | | | | | | | | | | | | |
| | 9916 | | | | | | | | E | P 1 | 998-9 | 3152 | 1 | 1998 | 0623 | | |
| EP | 9916 | | | | | | | | | | | | | | | | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR | , IT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | ΙE, | | | | | | | | | | | | | | | |
| | 2001 | | | | | 2001 | 1002 | | J | P 1 | 999-5 | 0499 | 7 | 19980 | 0623 | | |
| US | 6482 | 849 | | B | 1 | 20023 | 1119 | | U | S 1 | 998-1 | 0258 | 4 | 19980 | 0623 | | |
| AT | 2494 | 21 | | \mathbf{E} | | 20030 | 915 | | Z. | T 1 | 998-9 | 3152 | 1 | 19980 | 0623 | | |
| ES | 2206 | 953 | | T | 3 | 20040 | 0516 | | F | S 1 | 998-9 | 3152 | 1 | 19980 | 0623 | | |
| US | 2003. | 1303 | 49 | A. | 1 | | | | U | S 2 | 002-1 | 9313 | 7 | 20020 | 0712 | | |
| | 6596 | | | | | | | | | | | | | | | | |
| PRIORITY | Y APP | LN. | INFO | . : | | | | Ţ | JS 1 | 997. | -5051 | 5P | Ρ | 19970 | 0623 | | |
| | | | | | | | | Į. | JS 1 | 998- | -1025 | 84 | А3 | 19980 | 0623 | | |
| | | | | | | | | | | 998- | -US13 | 064 | W | 19980 | 0623 | | |
| OTHER SO | DURCE | (S): | | | MAR | PAT 1 | L30:9 | 95843 | 3 | | | | | | | | |

GΙ

Title compds. [I; n = 0, 1; R1 = H, CH3; R2 = CN, CO2H, CONH2, CONHOCH2Ph, AB NHCOOCH2Ph, etc.; R3 = H, CH3; X = CH, CO; R4 = H, alkyl; R5 = CO2H, CONH2, COOR, etc.; R = alkyl; R6 = aryl, heteroaryl, arylcarbonyl, aarylcarbonylaminoalkyl, etc.], a pharmaceutically acceptable salt, a stereoisomer thereof are prepared as inhibitors of $\alpha 4\,\beta 1$ mediated adhesion to either VCAM or CS-1 and which can be used for treating or preventing $\alpha 4\beta 1$ adhesion mediated conditions in human such as inflammatory diseases. Thus, (1S-cis) - N-[(3-carboxy-2,2,3trimethylcyclopentyl)carbonyl]-O-(phenylmethyl)-L-tyrosine was prepared and assayed for inhibition of β 1-mediated cell adhesion in vitro.

ΙT 219495-30-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of cyclopentylcarbonylamino acid as inhibitors of $\alpha 4\beta 1$ mediated cell adhesion)

RN 219495-30-4 HCAPLUS

L-Phenylalanine, N-[[(1S,3R)-3-carboxy-2,2,3-trimethylcyclopentyl]carbonyl CN 1-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 18 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:745015 HCAPLUS

DOCUMENT NUMBER:

130:3692

TITLE:

INVENTOR(S):

Preparation of ω-(salicyloylamino)alkanoic acids Gschneidner, David; O'Toole, Doris; Freeman, John

PATENT ASSIGNEE(S): SOURCE:

Emisphere Technologies, Inc., USA

PCT Int. Appl., 24 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

APPLICATION NO. DATE KIND DATE PATENT NO. _____ _____ WO 9850341 WO 1998-US8449 19980424 A1 19981112 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG 19991005 US 1997-853752 19970509 US 5962710 Α AU 1998-71641 19981127 AU 9871641 Α1 US 1997-853752 PRIORITY APPLN. INFO.: 19970509 WO 1998-US8449 19980424 CASREACT 130:3692; MARPAT 130:3692 OTHER SOURCE(S): The title method comprises salicyloylation of an ω -aminoalkanoate by HOZ1CO(OZ2CO) nOH [Z1, Z2 = (un) substituted C6H4; n = 1 to .apprx.10].209962-04-9P ΙT RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of ω -(salicyloylamino)alkanoic acids) 209962-04-9 HCAPLUS RN Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) CN (CA INDEX NAME)

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 19 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:548547 HCAPLUS

DOCUMENT NUMBER:

129:180147

TITLE:

Compounds and compositions for delivering active

agents

INVENTOR(S):

Leone-Bay, Andrea; et al.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE: PCT Int. Appl., 147 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

30

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| | | | | |
| WO 9834632 | A1 | 19980813 | WO 1998-US2619 | 19980206 |

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            DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR,
            KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
            ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
            FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
                                                            19970207
                                           US 1997-796337
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                                           AU 1998-62756
                                                            19980206
    AU 9862756
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                            19980826
                      В2
                            20010927
    AU 738735
                                           EP 1998-905042
                                                            19980206
                      Α1
                            20000705
    EP 1015008
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                                                            19980206
                                           JP 1998-535034
    JP 2001513080
                       T2
                            20010828
                                                            19980206
                                           NZ 1998-337131
                            20010831
    NZ 337131
                       Α
                                           MX 1999-7290
                                                            19990806
                            20000531
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                                           AU 2000-72261
                                                             20001214
                            20040311
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                       B2
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                       В2
                            20040325
                                           AU 2000-72260
    AU 771434
                                                            20001219
                                           US 2000-746548
    US 2002119910
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                            20020829
                                                            20011031
                                           US 2001-1731
    US 2003008900
                            20030109
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                       В2
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    US 6525020
                                           US 2003-373582
                                                            20030224
                       Α1
                            20031225
    US 2003235612
                                                             20030324
                                           US 2003-395685
    US 2004022856
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                                                         A1 19970207
                                        US 1997-796334
PRIORITY APPLN. INFO.:
                                                         A1 19970207
                                        US 1997-796335
                                                         A1 19970207
                                        US 1997-796336
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                                                         P 19960329
                                        US 1996-17902P
                                                         A2 19970318
                                        WO 1997-US5128
                                                         A3 19980206
                                        AU 1998-62756
                                                         A3 19980206
                                        EP 1999-117292
                                                         W 19980206
                                        WO 1998-US2619
                                                         B1 20001219
                                        US 2000-746548
                                                         A1 20011031
                                        US 2001-1731
AB
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AB Carrier compds. and compns. which are useful in the delivery of active agents are provided. The carrier compound can be an amino acid derivative, and the active agent can be a peptide, mucopolysaccharide, carbohydrate, or lipid. Methods of administration, including oral administration, and

preparation are provided as well. For example, an oral solution contained parathyroid hormone 100 $\mu g,\ 4\text{-}[4\text{-}(phenoxyacetyl)aminophenyl]butyric acid (as carrier) 400 mg, and water 1L.$

209961-45-5 209961-75-1 209961-80-8 209961-83-1 209961-85-3 209962-03-8 209962-04-9 209962-15-2 209962-17-4

211511-75-0 211511-91-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid derivs. as carriers for oral delivery of biol. active

agents)
RN 209961-45-5 HCAPLUS

CN Benzenebutanoic acid, 4-[[(1-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI)
(CA INDEX NAME)

RN 209961-75-1 HCAPLUS CN Benzenebutanoic acid, 4-[(2-hydroxy-5-iodobenzoyl)amino]- (9CI) (CA INDEX

RN 209961-80-8 HCAPLUS CN Benzenebutanoic acid, 4-[(5-chloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 209961-83-1 HCAPLUS CN Benzenebutanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

209961-85-3 HCAPLUS RN

Benzenepropanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]-CN (9CI) (CA INDEX NAME)

209962-03-8 HCAPLUS RN

Benzenebutanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA CN INDEX NAME)

209962-04-9 HCAPLUS RN

Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) CN (CA INDEX NAME)

209962-15-2 HCAPLUS RN

Benzeneacetic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA CN INDEX NAME)

209962-17-4 HCAPLUS RN

Benzenepentanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

211511-75-0 HCAPLUS RN

Benzenebutanoic acid, 4-[(4-bromo-2-hydroxybenzoyl)amino]- (9CI) (CA CN INDEX NAME)

211511-91-0 HCAPLUS RN

Benzenebutanoic acid, $4-[(2-hydroxybenzoyl)amino]-\gamma-oxo-(9CI)$ (CA CNINDEX NAME)

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS 7 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 20 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:481964 HCAPLUS

DOCUMENT NUMBER:

129:265258

TITLE: AUTHOR(S): Novel delivery agents for induction of oral tolerance Haas, S.; Meleski, D.; Kutzy, T.; Gerspach, L.;

Lercara, C.; O'toole, D.; Devincent, A.; Milstein, S.

CORPORATE SOURCE:

Emisphere, Technologies, Inc., Hawthorne, NY, 10532,

SOURCE:

Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998),

25th, 621-622

CODEN: PCRMEY; ISSN: 1022-0178 Controlled Release Society, Inc.

PUBLISHER: DOCUMENT TYPE:

Journal

LANGUAGE:

English

GI

A single oral dose of 1.0 mg/rat of myelin basic protein (MBP) + EMI-A (I) AB suppressed the development of clin. disease symptoms of MBP-induced encephalomyelitis to the same extent as five doses of 1.0 mg each of MBP alone, and significantly more than a single dose of MBP alone. Feeding rats 5 doses of 0.1 mg of MBP each in the presence of EMI-B (II) lowered the AUC of the disease course $\sim 60\%$ compared with MBP alone. This suggests that Emisphere's delivery agents may constitute an oral delivery system that can augment the inducing tolerance properties of co-administered proteins, allowing the use of fewer or lower doses than are generally required. This technol. may be useful in the treatment of autoimmune and allergic disorders and for the prevention of allograft rejection.

177653-18-8, EMI-A ΙT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(novel delivery agents for induction of oral tolerance)

177653-18-8 HCAPLUS RN

Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 3 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 21 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

1998:457247 HCAPLUS ACCESSION NUMBER:

129:113532 DOCUMENT NUMBER:

Compounds and compositions for delivering active TITLE:

agents

Leone-Bay, Andrea; Wang, Eric; Sarubbi, Donald J.; INVENTOR(S):

Leipold, Harry

Emisphere Technologies, Inc., USA PATENT ASSIGNEE(S):

SOURCE:

U.S., 34 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

| P | PAT | ENT NO. | | | DATE | | | | PPLI | CATIO | ОИ ИС |). | DATE | | | |
|-------|----------|--|---|----------------------------------|--|--------------------------|---------------------------------|---------------------------------|---------------------------------|----------------------------------|-------------------------|-------------------|----------------------------------|----------------------|-------------------|-------------------|
| | CA CA | 5776888 2319672 2319680 9834632 | | A AA AA | 1998(1998(1998(| 0707 0813 0813 | | U C C W | A 19 A 19 O 19 | 97-79 98-23 98-23 98-03 | 31967 31968 32619 | 72 30 9 | 1997(1998(1998(1998(| 0206 0206 0206 | | |
| · | • | W: AI DK KZ PI US | , AM, EE, , LC, , PT, , US, | ES, I LK, I RO, I US, I | AU, AZ, FI, GB, LR, LS, RU, SD, US, US, BY, KG, | GE, LT, SE, US, | GW, LU, SG, US, MD. | HU, LV, SI, US, RU, | ID, MD, SK, US, TJ, | IL, MG, SL, US, TM | MK, TJ, US, | MN, TM, US, | MW, TR, US, | MX, TT, UZ, | NO, UA, VN, | NZ, UG, YU, |
| | | FF | GB, | GR, | LS, MW, IE, IT, MR, NE, | LU, | MC, | NL, TG | PT, | SE, | BF, | Βυ, | CF, | CG, | CI, | CM, |
| Z | 17.4 | 9862756 | | A1 | | 0826 | | P | U 19 | 98-6 | 2756 | | 1998 | 0206 | | |
| | | 738735 | | В2 | 2001 | (1927 | | | | | | | | | | |
| | | 993831 | | . A2 | 2000 | | | E | IP 19 | 99-1 | 1729: | 2 | 1998 | 0206 | | |
| F | ΞP | 993831 | | А3 | 2001 | 0502 | | | | | | | | a n | MO | Dα |
| | | | BE, E, FI | CH, | DE, DK, | | | | | | | | | | MC, | P1, |
| Ι | EΡ | 1015008 | } | A1 | 2000 | 0705 | | E | EP. 19 | 98-9 | 0504 | 2 | 1998 | 0206 | | D.M. |
| | | R: A | BE, E, FI | CH, | DE, DK, | | | | | | | | | | MC, | PT, |
| ī | EР | 1093819 | | A2 | 2001 | 0425 | | F | EP 20 | 000-1 | 2270 | 4 | 1998 | 0206 | | |
| | | 1003810 | 3 | А3 | 2003 | 0514 | | | | | | | | | | |
| • | | R: A | r, BE, E, FI | CH, | DE, DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | σт. | 200113 | | A2 | 2001 | 0515 | | | JP 20 | 000-3 | 1123 | 1 | 1998 | 0206 | | |
| | | 200113 | | A2 | | | | | | 000-3 | | | 1998 | | | |
| | | 200151 | | Т2 | 2001 | 0828 | | | | 98-5 | | | 1998 | | | |
| | | 337131 | | А | 2001 | 0831 | | | | 998-3 | | 1 | | 0206 | | |
| | | 990729 |) . | A | 2000 | 0531 | | | | 999-7 | | | | 0806 | | |
| | ΝZ | 507275 | | A A | 2001 | 1130 | 1 | | | 000-5 | | | | 1003 | | |
| | | 507276 | | A | | 0201 | | | | 000-5 | | | 2000 | | | |
| | ΑU | 771024 | | В2 | | | | | | 000-7 | | | 2000 | | | |
| | | 771434 | | В2 | 2004 | 0325 | Ó | | | 000-7 | | | | 1214 0207 | | |
| PRIOR | ΙT | Y APPLN | . INFO | o.: | | | | | | -7963 | | A. | | 0207 | | |
| | | | | | | | | | | -7963 -7963 | | Α | | 0207 | | |
| | | | | | | | | US . | 1997. 1997. | -7963 -7963 | , , o o | Δ | | 0207 | | • |
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| | | | | | | | | OD. | エノント | 1000 | , , , | | , | | | |

US 1997-796339 A 19970207 US 1997-796340 19970207 Α 19970207 US 1997-796341 Α US 1997-797100 Α 19970207 US 1997-797813 19970207 Α US 1997-797816 19970207 Α US 1997-797817 19970207 Α A US 1997-797820 19970207 AU 1998-62756 A3 19980206 CA 1998-2279331 A3 19980206 A3 19980206 EP 1998-905042 A3 19980206 EP 1999-117292 JP 1998-535034 A3 19980206 Al 19980206 NZ 1998-337131 WO 1998-US2619 W 19980206

Carrier compds. and compns. which are useful in the delivery of active AΒ agents are provided. Methods of administration and preparation are provided as well. Standard methods of preparation are mentioned for the 193 carrier compds.

listed, which primarily are N-(fatty acid) benzamide derivs. Examples are listed for the delivery of parathyroid hormone, recombinant human growth hormone, interferon and the evaluation of heparin in rats.

209961-45-5P 209961-75-1P 209961-80-8P ΙT 209961-83-1P 209961-85-3P 209962-03-8P 209962-04-9P 209962-15-2P 209962-17-4P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of benzamide fatty acid derivs. for delivering active agents)

209961-45-5 HCAPLUS RN

Benzenebutanoic acid, 4-[[(1-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) CN (CA INDEX NAME)

209961-75-1 HCAPLUS RN Benzenebutanoic acid, 4-[(2-hydroxy-5-iodobenzoyl)amino]- (9CI) (CA INDEX CN

209961-80-8 HCAPLUS Benzenebutanoic acid, 4-[(5-chloro-2-hydroxybenzoyl)amino]- (9CI) (CA RN CN INDEX NAME)

RN 209961-83-1 HCAPLUS CN Benzenebutanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 209961-85-3 HCAPLUS CN Benzenepropanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]-(9CI) (CA INDEX NAME)

RN 209962-03-8 HCAPLUS CN Benzenebutanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 209962-04-9 HCAPLUS CN Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

209962-15-2 HCAPLUS RN

Benzeneacetic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA CNINDEX NAME)

209962-17-4 HCAPLUS RN

Benzenepentanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

REFERENCE COUNT:

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS 13 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 22 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:430107 HCAPLUS

DOCUMENT NUMBER:

129:113525

TITLE:

Compounds and compositions for delivering active

INVENTOR(S):

Leone-Bay, Andrea; Wang, Eric; Sarubbi, Donald J.;

Leipold, Harry

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 35 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------------------------|---------|----------------------|-----------------------------------|----------------------|
| | | | | |
| US 5773647 CA 2319672 | A AA | 19980630 19980813 | US 1997-796337 CA 1998-2319672 | 19970207 19980206 |

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CA 1998-2319680 19980206
                            19980813
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    CA 2319680
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                      Al
    WO '9834632
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR,
            KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, US, US, US, VN, YU,
            ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
            FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
             GA, GN, ML, MR, NE, SN, TD, TG
                                                             19980206
                                            AU 1998-62756
                      A1
                          19980826
    AU 9862756
                            20010927
                       В2
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                                            EP 1999-117292
                            20000419
                       Α2
    EP 993831
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                       А3
    EP 993831
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                                            EP 1998-905042
                                                             19980206
                            20000705
                       Α1
    EP 1015008
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                                            EP 2000-122704
                                                             19980206
                       Α2
                            20010425
    EP 1093819
                       А3
                            20030514
    EP 1093819
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                                            JP 2000-311231
                                                             19980206
                            20010515
    JP 2001131090
                       Α2
                                            JP 2000-311230
                                                             19980206
                            20010522
                       Α2
    JP 2001139494
                                            JP 1998-535034
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                            20010828
                       Т2
    JP 2001513080
                                                              19980206
                                            NZ 1998-337131
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    NZ 337131
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                                                              19990806
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                            20000531
    MX 9907290
                                            NZ 2000-507275
                                                              20001003
                             20011130
                       Α
     NZ 507275
                                            NZ 2000-507276
                                                              20001003
                             20020201
     NZ 507276
                       Α
                                                              20001214
                                            AU 2000-72261
                             20040311
                       В2
     AU 771024
                                                              20001214
                                            AU 2000-72260
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     AU 771434
                                                             19970207
                                                          Α
                                         US 1997-796334
PRIORITY APPLN. INFO.:
                                                           Α
                                                             19970207
                                         US 1997-796335
                                         US 1997-796336
                                                           Α
                                                             19970207
                                                              19970207
                                         US 1997-796337
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                                         US 1997-796338
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                                         US 1997-796339
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                                         US 1997-796340
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                                                              19970207
                                         US 1997-796341
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                                         US 1997-797100
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                                         US 1997-797813
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                                         US 1997-797816
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                                         US 1997-797817
                                                           A 19970207
                                         US 1997-797820
                                                           A3 19980206
                                         AU 1998-62756
                                          CA 1998-2279331 A3 19980206
                                                           A3 19980206
                                          EP 1998-905042
                                                           A3 19980206
                                          EP 1999-117292
                                                           A3 19980206
                                          JP 1998-535034
                                                           A1 19980206
                                          NZ 1998-337131
                                                           W 19980206
                                          WO 1998-US2619
     Carrier compds. and compns. therewith which are useful in the delivery of
AΒ
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AB Carrier compds. and compns. therewith which are useful in the delivery of active agents are provided. Methods of administration and preparation are provided as well. Standard methods of preparation are mentioned for the 193 carrier compds. listed, which primarily are N-(fatty acid) benzamide derivs. Examples are listed for the delivery of parathyroid hormone, recombinant human growth hormone, interferon and the evaluation of heparin in rats.

- RN 209961-45-5 HCAPLUS CN Benzenebutanoic acid, 4-[[(1-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 209961-75-1 HCAPLUS CN Benzenebutanoic acid, 4-[(2-hydroxy-5-iodobenzoyl)amino]- (9CI) (CA INDEX

RN 209961-80-8 HCAPLUS CN Benzenebutanoic acid, 4-[(5-chloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 209961-83-1 HCAPLUS CN Benzenebutanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 209961-85-3 HCAPLUS CN Benzenepropanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]-(9CI) (CA INDEX NAME)

RN 209962-03-8 HCAPLUS CN Benzenebutanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 209962-04-9 HCAPLUS CN Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 209962-15-2 HCAPLUS CN Benzeneacetic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

209962-17-4 HCAPLUS Benzenepentanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) RN CN

REFERENCE COUNT:

THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS 33 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 23 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:344628 HCAPLUS

DOCUMENT NUMBER:

129:36449

TITLE:

Methods and compositions using derivatized amino acids

for inducing oral tolerance in mammals

INVENTOR(S):

Haas, Susan; Milstein, Sam J.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA; Haas, Susan;

Milstein, Sam J.

SOURCE:

PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PA: | TENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---------|------------------------|---------|----------------------|---|---------------------------------|----|
| WO | 9821951 | | 19980528 | WO 1997-US14676 | 19970820 | |
| | W: CA, IL, RW: AT, BE, | CH, DE, | DK, ES, | FI, FR, GB, GR, IE, IT CA 1997-2243643 | , LU, MC, NL, PT, S 19970820 | 3E |
| | 2243643 | 7.1 | 19980528 19981230 | EP 1997-939468 | 19970820 | |
| EP | 886471 R: AT, BE, | CH, DE, | DK, ES, | FR, GB, GR, IT, LI, LU | , NL, SE, MC, PT, | |
| IIS | IE, FI 6391303 | В1 | 20020521 | US 1999-101921 | 19990503 | |
| US | 2002061311 | A1 | 20020523 | US 2001-17076 US 1996-31356P P | 20011214 19961118 | |
| PRIORIT | Y APPLN. INFC |).: | | US 1997-49691P P | 19970616 | |
| | | | | WO 1997-US14676 W US 1999-101921 A1 | 19970820 19990503 | |
| | | | | 00 1999 101911 | 1999000 | |

MARPAT 129:36449 OTHER SOURCE(S):

Methods and pharmaceutical formulations are provided for orally delivering an antigen to induce tolerance. The antigen is combined with derivatized amino acids or salts thereof. The induction of oral tolerance may be

applied clin. for the prevention or treatment of autoimmune diseases and clin. allergic hypersensitivities, and for the prevention of allograft rejection.

177653-18-8 ΙT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(derivatized amino acids for inducing oral tolerance)

177653-18-8 HCAPLUS RN

Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 24 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

2

ACCESSION NUMBER:

1998:313029 HCAPLUS

DOCUMENT NUMBER:

129:8535

TITLE:

Novel delivery agents for mucosal immunization Haas, S.; Meleski, D.; Kutzy, T.; Lercara, C.;

O'toole, D.; Leipold, H.

CORPORATE SOURCE:

Emisphere Technologies, Inc., Hawthorne, NY,

10532-2152, USA

SOURCE:

S.T.P. Pharma Sciences (1998), 8(1), 59-65

CODEN: STSSE5; ISSN: 1157-1489

PUBLISHER:

AUTHOR(S):

Editions de Sante

DOCUMENT TYPE:

Journal English

LANGUAGE:

Soluble, low mol. weight delivery agents provide a novel approach to the AB mucosal

delivery of antigens. These compds. are easily synthesized by conventional chemical methods, and may be dissolved directly in an antigen solution/suspension for convenient administration. Antigen-specific secretory IgA (fecal and salivary) and systemic responses (circulating anti-ovalbumin isotypes and antigen-specific delayed-type hypersensitivity) were induced by dosing ovalbumin together with various delivery agents either orally or colonically. The data suggest that delivery agents facilitate transport of antigenically intact ovalbumin through the mucosa of both the upper and lower gastro-intestinal tracts. The possible mechanism of action and potential applications are discussed.

IΤ 177653-18-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(delivery agents for mucosal immunization)

177653-18-8 HCAPLUS RN

Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

REFERENCE COUNT:

THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS 26 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 25 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1997:790387 HCAPLUS

DOCUMENT NUMBER:

128:106314

TITLE:

Acylated non- α -amino acids as novel agents for

the oral delivery of heparin sodium, USP

AUTHOR(S):

Leone-Bay, Andrea; Paton, Duncan R.; Variano, Bruce; Leipold, Harry; Rivera, Theresa; Miura-Fraboni, Judy;

Baughman, Robert A.; Santiago, Noemi

CORPORATE SOURCE:

Hawthorne, 15 Skyline Drive, Emisphere Technologies,

Inc., New York, 10532, USA

SOURCE:

Journal of Controlled Release (1998), 50(1-3), 41-49

CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER:

Elsevier Science B.V.

DOCUMENT TYPE:

Journal

LANGUAGE:

English Ten N-acylated, non-lpha-amino acids were prepared as oral delivery

agents and used to demonstrate the oral delivery of heparin in vivo in rats and primates. Following the oral administration of solns. containing a combination of heparin and a delivery agent to rats or primates, significant plasma heparin concns. were evidenced by APTT and anti-Factor Xa assays. The estimated pharmacodynamic equivalence for an oral dosing

solution

containing heparin and a delivery agent is 39 in primates. In vitro expts. based on heparin affinity chromatog. or heparin/methylene blue complexation were also performed to begin investigation of the mechanism by which these compds. facilitate heparin oral delivery. Results of in vitro studies suggest that absorption of the drug across the gastrointestinal membrane is the result of a noncovalent interaction between heparin and the delivery agent.

177653-18-8 ΙT

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (acylated non- α -amino acids for delivery of heparin)

177653-18-8 HCAPLUS

Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

REFERENCE COUNT:

THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS 20 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 26 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

DE, LC, PT, VN,

GB, GN,

ACCESSION NUMBER:

1997:672238 HCAPLUS

DOCUMENT NUMBER:

127:322800

TITLE:

Modified amino acids for drug delivery

INVENTOR(S):

Leone-Bay, Andrea

PATENT ASSIGNEE(S):

Emishphere Technologies, Inc., USA; Leone-Bay, Andrea

SOURCE:

PCT Int. Appl., 64 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

30

PATENT INFORMATION:

| PAT | ENT I | . O <i>r</i> | | KII | ND | DATE | | | F | PPLI | CATI | ON NO | o. | DATE | | |
|----------|-------------------|---------------------------------|---------------------------------|--|---------------------------------|-------------------------------------|---------------------------------|--------------------------|---------------------------------|--|---|---|--------------------------|------------------------------|--|-------------------|
| WO | 9736 W: RW: | AL, DK, LK, RO, YU, | EE, LR, RU, AM, KE, | AT, ES, LS, SD, AZ, LS, | AU, FI, LT, SE, BY, | KG, | BA, GE, LV, SI, KZ, | MU, MD, SK, MD, | BG, IL, MG, TJ, RU, | BR, IS, MK, TM, TJ, BE, | BY, JP, MN, TR, TM | CA, KE, MW, TT, | CH, KG, MX, UA, | NO, UG, ES, | CU, KR, NZ, US, | PL, UZ, FR, |
| AU AU | 7710 7714 | ML, 958 956 24 34 | MR, | NE, A A B | SN, 1 2 | TD, 2000 1997 2004 2004 | TG 0718 1022 0311 | | US US WO | JS 19 AU 19 AU 20 AU 20 1996- 1996- | 997-7 997-2 000-7 000-7 -1790 -1790 -US51 | 9781 5956 2261 2260 2 2P 28 | 6 A1 P A2 | 1997 1997 2000 2000 | 0207 0318 1214 1214 0329 0329 0318 | |

MARPAT 127:322800 OTHER SOURCE(S):

Modified amino acid compds. useful in the delivery of active agents are provided. E.g., 2HOC6H4CONH(CH2)7CO2H was prepared from 8-aminocaprylic acid and O-acetylsalicyloyl chloride. Also examples were give of a nol. of delivery agents enhancement of recombinant human growth hormone bioavailability administered s.c. in rats.

61126-74-7P 177653-30-4P 177653-62-2P IT

177653-64-4P 183990-74-1P

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(modified amino acids for drug delivery)

61126-74-7 HCAPLUS RN

Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

177653-30-4 HCAPLUS Benzenebutanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX RN CN NAME)

177653-62-2 HCAPLUS RN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

177653-64-4 HCAPLUS Benzenepropanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX RN CN NAME)

183990-74-1 HCAPLUS Butanedioic acid, [4-[(2-hydroxybenzoyl)amino]phenyl]- (9CI) (CA INDEX RN CN NAME)

L17 ANSWER 27 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: DOCUMENT NUMBER:

1997:527636 HCAPLUS

TITLE:

127:152958 Modified amino acid carriers, their preparation, and compositions containing them for delivering active

agents

INVENTOR(S):

Leone-Bay, Andrea; Paton, Duncan R.; Ho, Koc-Kan;

DeMorin, Frenel

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 231,622.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT: 30

English

OTHER SOURCE(S): MARPAT 127:152958

PATENT INFORMATION:

| | ENT | | | | | DATE | | | A: | PPLI | CATIO | М ИС | o. | DATE | | | | |
|----------------------------|--|---|-------------------------|--------|---------------|--------------|---|------------|--|--|----------------|---|----------------------------------|------------|--|------------|------------|----|
| US US US US CA | 5643 5451 5792 5629 2203 9612 W: | 957 410 451 020 033 473 AL, FI, MD, | AM, GB, MG, | AT, | A 1 AU, | TS. | 0701 0919 0811 0513 0502 0502 BG, | BR, | U: U: U: C: W: BY, KG. | 5 19 5 19 5 19 A 19 O 19 CA, KP, | KK, | 1019 0551 3162 2030 S135 CN, | 1 2 33 27 CZ, LK, | ъr, | 0422 0302 0422 1016 1016 DK, LT, | шо, | ш∨, | |
| | RW: | KE, LU, | TJ MW, MC, TD, | ΝL, | SZ, PT, | UG, SE, | AT, BF, | BE, BJ, | CH, CF, | DE, CG, | DK, CI, | ES, CM, | FR, GA, | GB, GN, | GR, ML, | IE, MR, | IT, NE, | |
| ΑIJ | 9539 | | 10, | A | 1 | 1996 | 0515 | | А | U 19 | 95-3 | 9633 | | 1995 | 1016 | | | |
| | 7118 | | | В | | 1999 | | | יז | n 10 | 95-9 | 3755 | R | 1995 | 1016 | | | |
| | 7832 7832 | 0.0 | | A B | 1 | 1997 | na1 n | | | | | | | | | | | |
| ĽР | 7032 R: | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IE, | IT, | LI, | LU, | MC, | NL, | PT, | SE |
| | 9510 | 168 | | A | | 1997 | 1014 | | В | R 19 | 95 - 1 | ΛTρα | | 1990 | 1016 | | | |
| | 7775 | |) | | .2 2 | 1998 1998 | | | | | 95-5 | | 2 | | 1016 | | | |
| | 1050 2494 | | • | E | | | 0915 | | P | T 19 | 95-9 | 3755 | 8 | | 1016 | | | |
| | 2207 | | | T | 3 | 2004 | 0601 | | | | 95-9 | | | | 1016 | | | |
| | 5955 | | | A | | | 0921 | | | | 97-7 | | | | '0206 '0206 | | | |
| | 6100 | | | A | | | 0808 | | | | 97-7 97-1 | |) / | | 0424 | | | |
| | 9701 | | | P. | | | '0623 '0425 | | | | 97-1 | | | | 0425 | | | |
| | 9701 2001 | | 101 | | 1 | | .0607 | | | | 00-7 | | 6 | 2000 | 1205 | | | |
| - | 7710 | |) () L | | 32 | | 0311 | | P | U 20 | 00-7 | 2261 | L | 2000 | 1214 | | | |
| | 7714 | | | | 32 | | 0325 | | | | 000-7 | | | |)1214 | | | |
| | 2002 | | 009 | P | 1 | | 20829 | | Ţ | IS 20 | 002-9 | 90012 | 2 | 2002 | 20221 | | | |
| | 6663 | | | | 32 | | 31216 | | T | 10 O(| 003-6 | 7790 | 16 | 2003 | 31001 | | | |
| | 2004 | | | | 1 | 2004 | 10408 | i | | | -5101 | | | 1993 | | | | |
| IORIT | Y API | PLN. | INFC |).: | | | | | | | -2055 | | | 1994 | | | | |
| | | | | | | | | | | | -2316 | | | 1994 | | | | |
| | | | | | | | | | | | -US45 | | A2 | 1994 | 10422 | • | | |
| | | | | | | | | | | | -3351 | | | 1994 | | | | |
| | | | | | | | | | | | -US13 | | | 199 | | | | |
| | | | | | | | | | | | -7958 | | | 199 199 | | | | |
| | | | | | | | | | | | -6275 -3469 | | | 199 | | | | |
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Page 54

GI

Modified amino acid compds. useful in the delivery of active agents AΒ (peptides, carbohydrates, antigens, monoclonal antibodies, hormones, pesticides, etc.) are provided. Methods of administration and preparation are also provided. The effect of a composition containing e.g. interferon- $\alpha 2$ and e.g. I (preparation given) on the serum interferon level was determined ΙT

Ι

177653-18-8P 177653-26-8P RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(modified amino acid carrier preparation and compns. containing them for delivering active agents)

177653-18-8 HCAPLUS RN

Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

177653-26-8 HCAPLUS Benzenebutanoic acid, 4-[(2,4-dihydroxybenzoyl)amino]- (9CI) (CA INDEX RN NAME)

178558-94-6

RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(modified amino acid carrier preparation and compns. containing them for delivering active agents)

178558-94-6 HCAPLUS RN

Benzenebutanoic acid, 4-[[(2',5'-difluoro-3-hydroxy[1,1'-biphenyl]-4-CN yl)carbonyl]amino]- (9CI) (CA INDEX NAME)

L17 ANSWER 28 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1997:146141 HCAPLUS

DOCUMENT NUMBER:

126:263909

TITLE:

Solution phase preparation of highly pure amide

mixtures via in-situ chlorotrimethylsilane protection

and activation

AUTHOR(S):

Ho, Koc-Kan; Wang, Nai Fang; Lercara, Christine;

O'Toole, Doris C.; Achan, Douglas M.; Vuocolo, Edmund

A.; Leone-Bay, Andrea

CORPORATE SOURCE:

Emisphere Technol. Inc., Hawthorne, NY, 10532, USA Synthetic Communications (1997), 27(5), 883-895

SOURCE:

CODEN: SYNCAV; ISSN: 0039-7911

PUBLISHER:

Dekker

DOCUMENT TYPE:

Journal

LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 126:263909

GΙ

Coupling of 4-(4-aminophenyl)butyric acid with acyl halides in both organic and aqueous media were found to produce large amount of oligomeric materials. AΒ By using an in situ chlorotrimethylsilane protection/activation procedure, these oligomers were suppressed completely and the desired 4-(4-acylaminophenyl)butyric acids, e.g. I, were obtained in good yield and high purity. The method was also extended to a parallel synthesis of a three component mixture 1H-NMR of the mixture indicated that each component was formed in a nearly stoichiometric quantity.

177653-18-8P IΤ

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (acylamino)benzenebutanoates via protection and activation with chlorotrimethylsilane)

177653-18-8 HCAPLUS RN

Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME) CN

REFERENCE COUNT:

THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS 11 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 29 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1997:87 HCAPLUS

DOCUMENT NUMBER:

126:31174

TITLE:

Preparation of modified amino acid compounds for

delivering active agents

INVENTOR(S):

Leone-Bay, Andrea; Ho, Koc-Kan; Sarubbi, Donald J.; Milstein, Sam J.; Press, Jeffery Bruce

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA; Leone-Bay, Andrea; Ho, Koc-Kan; Sarubbi, Donald, J.; Milstein, Sam, J.;

Press, Jeffery, Bruce

SOURCE:

PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

| PATENT NO. | KIND DATE | APPLICATION NO. | DATE |
|---|---|--|--|
| W: AL, AM, ES, FI, LU, LV, | A1 19961003 AT, AU, AZ, BB, BG, GB, GE, HU, IS, JP, MD, MG, MK, MN, MW, | KE, KG, KP, KR, KZ, | LK, LR, LS, LT, |
| IE, IT, US 5650386 CA 2214323 AU 9656629 | MW, SD, SZ, UG, AT, LU, MC, NL, PT, SE, A 19970722 AA 19961003 A1 19961016 B2 19991104 | US 1995-414654 CA 1996-2214323 AU 1996-56629 | 19950331 19960401 19960401 |
| EP 817643 R: AT, BE, | A1 19980114 CH, DE, DK, ES, FR, | GB, GR, 1T, L1, LU, | NL, SE, MC, II, |
| RU 2203268 JP 2003313157 US 5965121 US 5989539 US 6001347 FI 9703828 NO 9704495 US 2001023240 US 6428780 US 6346242 AU 771024 | A 19991214 A 19970929 A 19971128 A1 20010920 B2 20020806 B1 20020212 B2 20040311 B2 20040325 | JP 2003-140962 US 1997-798023 US 1997-798032 US 1997-798031 FI 1997-3828 NO 1997-4495 US 1999-305506 US 2000-499958 AU 2000-72261 AU 2000-72260 | 19960401 19970206 19970206 19970206 19970929 19970929 19990505 20000208 20001214 |

| US 6623731 US 2003078302 US 6699467 | B2 A1 B2 | 2003 | 30923 30424 30302 | | US 2002-14200 | 9 | 20020508 |
|---|----------------|------|-------------------------|-----|---------------|----|----------|
| US 2004110839 | A1 | | 0610 | | US 2003-62314 | 2 | 20030718 |
| PRIORITY APPLN. INFO.: | | 200. | | US | 1995-414654 | Α2 | 19950331 |
| | | | | US | 1995-3111P | Р | 19950901 |
| | | | | US | 1996-17902P | P | 19960329 |
| | | | | JΡ | 1996-529751 | АЗ | 19960401 |
| | | | | WO | 1996-US4580 | W | 19960401 |
| | | | | US | 1997-798031 | A1 | 19970206 |
| | | | | AU | 1998-62756 | ΑЗ | 19980206 |
| | | | | US | 1999-305506 | A1 | 19990505 |
| | | | | US | 2000-499958 | A1 | 20000208 |
| | | | | US | 2001-38426 | A1 | 20011019 |
| OTHER SOURCE(S): | MA | RPAT | 126:313 | L74 | | | |

OTHER SOURCE(S):

GΙ

$$HO_2C$$
 NH
 X
 II

Modified amino acid compds. [I (n = 0-3; m = 0-4; X = H, halo, OH, etc.), AΒ II (n = 0-3; X = 2-F, 3-MeO, 4-Me, etc.), etc.], useful in the delivery of active agents such as, e.g., human growth hormone, interferon, heparin, calcitonin, parathyroid hormone, were prepared Thus, reaction of 8-aminocaprylic acid with O-acetylsalicyloyl chloride in the presence of 2M aqueous NaOH afforded 57% III which was mixed with recombinant growth hormone (rhGH) in a phosphate buffer solution at pH 7-8 and administered orally to rats at 25 mg/kg of carrier and at 1 mg/kg of rhGH. The mean peak serum level of compound III was 60.92 ng/mL as compared to < 10 ng/mL for control.

61126-74-7P 177653-30-4P 177653-62-2P IT 177653-64-4P 183990-68-3P 183990-74-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of modified amino acid compds. for delivering active agents)

RN 61126-74-7 HCAPLUS

CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 177653-30-4 HCAPLUS

CN Benzenebutanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 177653-62-2 HCAPLUS

CN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 177653-64-4 HCAPLUS

CN Benzenepropanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 183990-68-3 HCAPLUS

CN Benzenebutanoic acid, 4-[[(2',4'-difluoro-4-hydroxy[1,1'-biphenyl]-3-yl)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 183990-74-1 HCAPLUS

CN Butanedioic acid, [4-[(2-hydroxybenzoyl)amino]phenyl]- (9CI) (CA INDEX NAME)

L17 ANSWER 30 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1996:562097 HCAPLUS

DOCUMENT NUMBER:

125:256974

TITLE:

Interaction of heparin with aromatic compounds: analysis of heparin affinity chromatography, equilibrium dialysis and circular dichroism

spectroscopy

AUTHOR(S):

Liao, Jun; Zhao, Ruifeng; Milstein, Sam; Ottenbrite,

Raphael M.

CORPORATE SOURCE:

High Technology Materials Center, Virginia

Commonwealth University, Richmond, VA, 23284-2006, USA Polymer Preprints (American Chemical Society, Division

SOURCE:

of Polymer Chemistry) (1996), 37(2), 157-158

CODEN: ACPPAY; ISSN: 0032-3934

PUBLISHER:

American Chemical Society, Division of Polymer

Chemistry

DOCUMENT TYPE:

Journal

LANGUAGE:

found

English

AB Clin. heparin (I) has to be administered via injection since the mol. structure, along with its biol. activities, is sensitive to the components in the gastrointestinal tract. Therefore, to develop an oral delivery system for I is important. A number of low mol. weight aromatic compds. were

to facilitate transport of heparin and protein drugs across the gastrointestinal epithelium and facilitated the oral delivery of these drugs to rats and primates. It was further revealed that these aromatic compds. interact with protein drugs, such as rhGH (recombinant human growth hormone), rhIFn (recombinant human $\alpha\text{-interferon})$, insulin, and that the interaction induces a reversible denaturalization of the native conformation of the drugs. The study of the interaction of heparin with the aromatic compds. E452, E445, and E352, was studied using I affinity chromatog., equilibrium dialysis and CD spectroscopy.

IT **177653-18-8**, E 352

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(interaction of heparin with aromatic compds.: anal. of heparin affinity chromatog., equilibrium dialysis and CD spectroscopy)

RN 177653-18-8 HCAPLUS

CNBenzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

L17 ANSWER 31 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1996:425385 HCAPLUS

DOCUMENT NUMBER:

125:96071

TITLE:

Modified amino acids as absorption enhancers for

delivering active agents

INVENTOR(S):

Leone-Bay, Andrea; Paton, Duncan R.; Ho, Kok-Kan;

Demorin, Frenel

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

| PA | PATENT NO. | | | KI | KIND DATE APPLICATION NO. DATE | | | | | | | | | | | | | |
|--------|--------------|-------|-------|------|--------------------------------|------|------|-----|-----|-------|-------|-------|-----|----------------|------|-------|-----|----|
| WO | 9612 | 473 | | A | 1 | 1996 | 0502 | | | | | | 27 | 19951016 | | | | |
| | | | | | | | | | | | | | | DE, | | | ES. | |
| | | | | | | | | | | | | | | LR, | | | | |
| | | | | | | | | | | | | | | SD, | | | | |
| | | SK, | | , | , | , | , | , | , | , | | , | , | , | , | , | , | |
| | RW: | KE, | MW, | SD, | SZ, | UG, | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙE, | ΙT, | |
| | | LU, | MC, | NL, | PT, | SE, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | ML, | MR, | NE, | |
| | | | TD, | | | | | | | | | | · | • | · | | · | |
| US | 5643 | 957 | | Α | | 1997 | 0701 | | U | S 199 | 94-3 | 3514 | 8 | 1994 | | | | |
| AU | 9539 | 633 | | A. | 1 | 1996 | 0515 | | A | J 199 | 95-3 | 9633 | | 1995 | 1016 | | | |
| | 7118 | | | | | | | | | | | | | | | | | |
| | 7832 | | | | | | | | E | P 199 | 95-93 | 3755 | 8 | 1995 | 1016 | | | |
| EΡ | 7832 | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | LU, | | NL, | PT, | SE |
| BR | 9510 | 168 | | A | • | 1997 | 1014 | | B | R 199 | 95-10 | 0168 | _ | 1995 | 1016 | | | |
| JP | 1050 2494 | 7762 | | T | 2 | 1998 | 3728 | | J. | P 199 | 95-5 | 1406: | 2 | 1995 | 1016 | | | |
| | | | | | | | | | | | | | | | | | | |
| NO | 9701 | 889 | | A | | 1997 | 0623 | | N(|) 199 | 97-18 | 389 | | 1997 | | | | |
| | 9701 | | | | | | | | | | | | | | | | | |
| | 7710: | | | | | | | | | | | | | 2000 | | | | |
| | 7714 | | | | | | | | | | | | | 2000 | | | | |
| RIORIT | I APP. | LN | LNEO | . : | | | | , | | | | | | 1994: 1993: | | | | |
| | | | | | | | | | | | | | | 1994 | | | | |
| | | | | | | | | | | | | | | 1994 | | | | |
| | | | | | | | | | | | | | | 1995 | | | | |
| | | | | | | | | | | | | | | 1998 | | | | |
| 3 Mod | difie | d ami | ino a | acid | com | pds. | as a | | | | | | | | | in tl | ne | |

delivery of active agents. These compound are used as carriers to facilitate the delivery of a cargo to a target. Thus, 47.00 g acetylsalicyloyl chloride was added to a mixture of 50.00 g 4-(4-aminophenyl)butyric acid in 300 mL of 2M aqueous sodium hydroxide and the reaction was stirred at 25° for 2 h, then it was acidified with aqueous HCl to obtain a precipitate which was separated and washed to give 31.89 g 4-(2-hydroxyphenylcarbonylamino)p-phenylbutanoic acid (I). I was mixed with interferon α -2 (II) in Tris-HCl buffer pH = 7-8 and was orally administered to rats at a rate of 300 mg I/kg and 1000 μg II/kg. The mean peak serum level of II was 8213 as compared to 688 ng/mL for controls.

IT 177653-18-8P 177653-26-8P 178558-94-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(modified amino acids as absorption enhancers for delivering active agents)

RN 177653-18-8 HCAPLUS

CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 177653-26-8 HCAPLUS

CN Benzenebutanoic acid, 4-[(2,4-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 178558-94-6 HCAPLUS

CN Benzenebutanoic acid, 4-[[(2',5'-difluoro-3-hydroxy[1,1'-biphenyl]-4-yl)carbonyl]amino]- (9CI) (CA INDEX NAME)

L17 ANSWER 32 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN ACCESSION NUMBER: 1996:326446 HCAPLUS

DOCUMENT NUMBER:

125:18819

TITLE:

4-[4-[(2-Hydroxybenzoyl)amino]phenyl]butyric Acid as a Novel Oral Delivery Agent for Recombinant Human Growth

Hormone

AUTHOR(S):

Leone-Bay, Andrea; Ho, Koc-Kan; Agarwal, Rajesh; Baughman, Robert A.; Chaudhary, Kiran; DeMorin, Frenel; Genoble, Lise; McInnes, Campbell; Lercara,

Christine; et al.

CORPORATE SOURCE:

SOURCE:

Emisphere Technologies Inc., Hawthorne, NY, 10532, USA

Journal of Medicinal Chemistry (1996), 39(13),

2571-2578

CODEN: JMCMAR; ISSN: 0022-2623 American Chemical Society

PUBLISHER: DOCUMENT TYPE:

Journal English

DOCUMENT TYPE: LANGUAGE:

As series of N-acetylated, non-α, aromatic aminocarboxylic acids was prepared and shown to promote the absorption of recombinant human growth hormone (rhGH) from the gastrointestinal tract. Seventy compds. in this family were tested in vivo in rats. Of the compds. tested, 4-[4-[(2-hydroxybenzoyl)amino]phenyl]butyric acid was identified as a preclin. candidate and was used to demonstrate the oral delivery of rhGH in primates. A significant pos. correlation was found between the relative log k' of the delivery agents, as determined by HPLC on an immobilized artificial membrane (IAM) column, and serum rhGH concns. following oral or colonic dosing in rats. Structure-activity relationships were also developed on the basis of electronic effects and hydrogen-bonding characteristics of the aromatic amide substituents.

IT 61126-74-7 177653-18-8 177653-26-8 177653-30-4 177653-62-2 177653-64-4

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hydroxybenzoylaminophenylbutyrate as oral vehicle for human growth hormone)

RN 61126-74-7 HCAPLUS

CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 177653-18-8 HCAPLUS

CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 177653-26-8 HCAPLUS

CN Benzenebutanoic acid, 4-[(2,4-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 177653-30-4 HCAPLUS

CN Benzenebutanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 177653-62-2 HCAPLUS

CN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 177653-64-4 HCAPLUS

CN Benzenepropanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

L17 ANSWER 33 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1977:5402 HCAPLUS

DOCUMENT NUMBER:

86:5402

TITLE:

Synthesis of quinazolinone and benzoxazinone acids and

study of their antiinflammatory properties

AUTHOR(S):

Picciola, G.

CORPORATE SOURCE:

Lab. Ric., Maggioni e C. S.p.A., Milan, Italy

SOURCE:

#

Farmaco, Edizione Scientifica (1976), 31(9), 655-64

CODEN: FRPSAX; ISSN: 0430-0920

DOCUMENT TYPE:

LANGUAGE:

Journal Italian GΙ

$$\begin{array}{c|c} O \\ N \\ X \\ R1 \end{array}$$

AB Quinazolinylphenylacetic acids I (X = N:CH, N:CMe, N:CPr; R = H, Me; R1 = H, C1; R2 = H, Et), I (X = NHCH2, NHCHMe; R = H, Me; R1 = H; R2 = H, Et), benzoxazinephenylacetic acids I (X = OCH2; R = H, Me; R1 = H, C1; R2 = H, Et), and 3.4-R1(2-HOC6H4CONH)C6H3CHRCO2R2 (R = H, Me; R1 = H, C1; R2 = H, Et) were prepared by various methods. None of the compds. showed any antiinflammatory activity.

IT 61126-74-7P 61126-76-9P 61126-78-1P 61126-80-5P

Ι

RN 61126-74-7 HCAPLUS

CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 61126-76-9 HCAPLUS

CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- α -methyl- (9CI) (CA INDEX NAME)

RN - 61126-78-1 HCAPLUS

CN Benzeneacetic acid, 3-chloro-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

RN 61126-80-5 HCAPLUS CN Benzeneacetic acid, 3-chloro-4-[(2-hydroxybenzoyl)amino]- α -methyl-(9CI) (CA INDEX NAME)

Inventor Search

Russel 10/617,266

12/07/2004

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=> d ibib abs hitstr 125 1-37
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L25 ANSWER 1 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2002:964132 HCAPLUS

DOCUMENT NUMBER:

138:29141

TITLE:

Compound and composition for delivering

biologically active agents, such

as parathyroid hormone

INVENTOR(S):

Leone-Bay, Andrea

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 26 pp. CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                   KIND DATE
                                       APPLICATION NO. DATE
                    ____
                                        -----
    WO 2002100338 A2
                          20021219
                                        WO 2002-US18236 20020607
    WO 2002100338
                    A3 20040212
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                     US 2001-297117P P 20010608
PRIORITY APPLN. INFO.:
```

AB Compds. and compns. for the **delivery** of biol. **active agents**, i.e., a protein, polypeptide, peptide, hormone,

polysaccharide, mucopolysaccharide, carbohydrate, or lipid, are provided.

These compds. are well suited for forming non-covalent mixts. with

active agents for oral, pulmonary, and other routes of

administration. Methods for the preparation and administration of such compns. are provided as well. For example, a **delivery** agent,

9-(4-hydroxybenzoylamino)nonanoic acid (I), was prepared from 1.17 equivalent

of

mL).

8-aminononanoic acid and 1.00 equivalent of 4-hydroxybenzoyl chloride and used for oral/intracolonic **delivery** of human parathyroid hormone residues 1-34 (PTH) by mixing I with a PTH stock solution (typically having a concentration of 5 mg PTH/mL) and diluting to the desired volume (usually 3.0

L25 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2001:526048 HCAPLUS

DOCUMENT NUMBER:

135:122313

TITLE:

Synthesis of benzoylaminophenyl derivatives for

delivering active agents

INVENTOR(S):

Boyd, Maria Aurora P.; Leone-Bay, Andrea;

O'Toole, Doris C.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 55 pp.

DOCUMENT TYPE:

CODEN: PIXXD2

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                     KIND DATE
                                          APPLICATION NO. DATE
                                          _____
                           _____
     WO 2001051454
                      A1
                            20010719
                                          WO 2001-US1274
                                                           20010112
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
             SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                      A1 20021009
                                         EP 2001-908609 20010112
     EP 1246792
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2003528822
                      T2
                            20030930
                                          JP 2001-551836
                                                           20010112
     US 2003149296
                      Α1
                            20030807
                                          US 2002-181275
                                                           20020805
PRIORITY APPLN. INFO.:
                                                           20000113
                                       US 2000-175947P P
                                       US 2000-194421P P
                                                           20000404
                                       US 2000-202210P P
                                                           20000505
                                       WO 2001-US1274
                                                        W 20010112
OTHER SOURCE(S):
                        MARPAT 135:122313
GΙ
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Title compds. I [R1-5 = H, halo, OH, OMe, alkyl, NH2, NHMe, NMe2 or NO2; n = 0 - 4; R6 = C6H4-O-R7-COOH optionally substituted with OH, OMe, alkyl, NH2, NHMe, NMe2, NO2, where R7 = alkyl] were prepared for use as delivery compds. for active agents. Eleven synthetic examples were provided. 2-Amino-4-chlorophenol was O-alkylated with Et 4-bromo butyrate. The intermediate ester was N-acylated with acetylsalicyloyl chloride and saponified to give II. Formulations of delivery compds./actives (e.g. insulin, parathyroid hormone, interferon, etc.), their (oral) administration and determination of serum concentration

over time were described. A formulation containing 200 mg/kg II and 0.5 mg/kg insulin administered orally (Sprague-Dawley rats) gave a mean peak serum

insulin concentration of 110.59 \pm 11.84 pg/mL. Oral administration of insulin without the drug delivery agent revealed no measurable levels of serum insulin.

REFERENCE COUNT:

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2001:338308 HCAPLUS

DOCUMENT NUMBER:

134:357556

TITLE:

Phenyl amine carboxylic acid compounds and

compositions for delivering active

agents

INVENTOR(S):

Leone-Bay, Andrea; Kraft, Kelly; Boyd, Maria

A. P.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 41 pp. CODEN: PIXXD2

Patent

DOCUMENT TYPE: LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| | PAT | rent : | NO. | | KI | ND | DATE APPLICATION NO. | | | | | | 0. | DATE | | | | |
|------|------|--------|------|------|----|------------------------|----------------------|------|------|-----------------------|------|------|------|------|-------|------|-----|-----|
| | | | | | | A2 200105 A3 200203 | | | | WO 2000-US41960 20001 | | | | | | 1106 | | |
| | | | | | | | | | AZ, | вА, | BB, | BG, | BR, | BY, | BZ, | CA, | CH, | CN, |
| | | | | | | | | | | | | | | | HR, | | | |
| | | | | | | | | | | | | | | | LT, | | | |
| | | | | | | | | | | | | | | | RU, | | | |
| | | | | | | | | | | | | | | | VN, | | | |
| | | | | | | | KΖ, | | | | | , | · | | · | • | | |
| | | RW: | | | | | | | | | | TZ, | UG, | ZW, | AT, | BE, | CH, | CY, |
| | | | | | | | | | | | | | | | PT, | | | |
| | | | | | | | | | | | | | | | TD, | | | |
| | ΑU | 2001 | | | | | | | | | | | | | | | | |
| | ΕP | 1226 | 109 | | А | 2 | 2002 | 0731 | | E | P 20 | 00-9 | 8976 | 1 | 2000 | 1106 | | |
| | | | | | | | | | | | | | | | ΝL, | | MC, | PT, |
| | | | | | | | | | | | ΑL, | | | | | | | |
| | JΡ | 2004 | 5010 | 57 | Т | 2 | 2004 | 0115 | | J | P 20 | 01-5 | 3433 | 8 | 2000 | | | |
| | ZA | 2002 | 0023 | 65 | A | | 2002 | 1025 | | Z | A 20 | 02-2 | 365 | | 20020 | 0325 | | |
| PRIO | RIT: | Y APP | LN. | INFO | .: | | | | | US 1 | 999- | 1638 | 06P | | 1999 | | | |
| | | | | | | | | | | US 2 | 000- | 2318 | 36P | | 2000 | | | |
| | | | | | | | | | | US 2 | 000- | 2372 | 33P | _ | 2000 | | | |
| | | | | | | | | | | | 000- | US41 | 960 | M | 2000 | 1106 | | |
| OTHE | R S | OURCE | (S): | | | MAR | PAT | 134: | 3575 | 56 | | | | | | | | |

Phenylaminecarboxylic acid compds. and compns. for the delivery AΒ of active agents are provided. E.g., I was prepared and used for oral delivery of drugs such as insulin.

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L25 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
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2001:297631 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 134:316090

Active agent transport systems TITLE:

Milstein, Sam J.; Leone-Bay, Andrea INVENTOR(S): ; Sarubbi, Donald J.; Leipold, Harry

Emisphere Technologies, Inc., USA

PATENT ASSIGNEE(S): U.S., 73 pp., Cont.-in-part of U.S. 6,099,856.

CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE:

SOURCE:

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

| | | DATE | APPLICATION NO. DATE |
|--------------------|----------|----------------------|---|
| us 6221367 | В1 | 20010424 | US 1997-939939 19970929 |
| US 5443841 | A | 19950822 | US 1992-920346 19920727 |
| US 5451410 | A | 19950919 | US 1993-51019 19930422 |
| US 5578323 | А | 19961126 | US 1993-76803 19930614 |
| US 5447728 | А | 19950905 | US 1993-168776 19931216 |
| US 5792451 | A | 19980811 | US 1994-205511 19940302 |
| US 5541155 | A | 19960730 | US 1994-231623 19940422 |
| US 5629020 | A | 19970513 | US 1994-231622 19940422 |
| US 5693338 | A | 19971202 | US 1994-315200 19940929 |
| US 6331318 | В1 | 20011218 | US 1994-316404 19940930 |
| ZA 9408342 | A | 19950622 | ZA 1994-8342 19941024 |
| US 5714167 | Α | 19980203 | US 1994-328932 19941025 |
| US 6099856 | A | 20000808 | US 1996-763183 19961210 |
| | В1 | 20020205 | US 1997-820694 19970318 |
| CA 2304951 | AA | 19990408 | CA 1998-2304951 19980929 |
| WO 9916427 | Al | 17770100 | WO 1998-US20548 19980929 |
| W: AL, AM, | AT, AU | , AZ, BA, | BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, |
| DK, EE, | ES, FI | , GB, GD, | GE, HR, HU, ID, IL, IS, JP, KE, KG, KP, |
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| | | , ML, MR, | NE, SN, TD, TG |
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| | | 20011108 | US 2001-760307 20010111 US 2001-5511 20011107 |
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| US 2002155993 | A1 | 20021024 20031216 | 02 2002-123030 20020413 |
| US 6663898 | | | US 2003-443713 20030521 |
| US 2003198658 | | 20031023 | US 1992-898909 B2 19920615 |
| IORITY APPLN. INFO | • • | | US 1992-920346 A2 19920727 |
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| | | | US 1993-143571 B2 19931026 |
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US 1996-17902P P 19960329
US 1996-763183 A2 19961210
US 1997-820694 A2 19970318
US 1997-939939 A 19970929
AU 1998-62756 A3 19980206
WO 1998-US20548 W 19980929
US 2001-929530 Al 20010813
US 2002-125836 A1 20020419
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Methods for transporting a biol. active agent across a AΒ cellular membrane or a lipid bilayer includes the steps of: (a) providing a biol. active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. active agent to a complexing perturbant to reversibly transform the biol. active agent to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. active agent across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. active agent. In the present invention, the biol. active agent does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. active agent comprising steps (a) and (b) above is also provided as are oral delivery compns. Addnl., mimetics and methods for preparing mimetics are contemplated. One example gives penetrant phenylsulfonyl-p-aminobenzoic acid effect on α -interferon.

REFERENCE COUNT:

THERE ARE 721 CITED REFERENCES AVAILABLE FOR 721 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L25 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
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ACCESSION NUMBER: 2000:608713 HCAPLUS

DOCUMENT NUMBER:

133:213157

TITLE:

SOURCE:

Aromatic amides for delivering

active agents

INVENTOR(S):

Tang, Pingwah; Leone-Bay, Andrea;

Gschneidner, David

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

APPLICATION NO. DATE KIND DATE PATENT NO. _____

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WO 2000-US4830
    WO 2000050386
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             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
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             KZ, MD, RU, TJ, TM
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    US 6646162
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PRIORITY APPLN. INFO.:
                                        US 1999-121850P P 19990226
                                        WO 2000-US4830 W 20000225
OTHER SOURCE(S):
                       MARPAT 133:213157
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AΒ Amides such as I are used for the delivery of active agents such as growth hormones. I was prepared from carsalam and 6-dimethylamino-1-hexanol, Ph3P, and diisopropyl azodicarboxylate in THF. Examples were given showing oral delivery of salmon calcitonin, low mol. wt heparin and human growth hormone with the addition of I. REFERENCE COUNT: THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:547374 HCAPLUS

DOCUMENT NUMBER:

133:155438

TITLE:

Active agent transport systems

comprising amino acids

INVENTOR(S):

Milstein, Sam J.; Barantsevitch, Evgueni;

Leone-Bay, Andrea; Wang, Nai Fang; Sarubbi, Donald J.; Santiago, Noemi B.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 71 pp., Cont.-in-part of U.S. 5,714,167.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| US 5451410 | А | 19950919 | US 1993-51019 | 19930422 |

US 1993-76803

US 5578323

Α

19961126

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             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ,
             VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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             GA, GN, ML, MR, NE, SN, TD, TG
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PRIORITY APPLN. INFO.:
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                                        US 1994-231623
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                                        US 1997-820694
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                                        US 1997-939939
                                                         A1 19970929
                                        WO 1997-US23545 W 19971209
                                        AU 1998-62756
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                                        US 1999-420200
                                                         A1 19991018
                                        US 2001-929530
                                                         A1 20010813
                                        US 2002-125836
                                                        A1 20020419
OTHER SOURCE(S):
                        MARPAT 133:155438
    Methods for transporting a biol. active agent across a
    cellular membrane or a lipid bilayer. A first method includes the steps
    of: (a) providing a biol. active agent which can exist
    in a native conformational state, a denatured conformational state, and an
    intermediate conformational state which is reversible to the native state
    and which is conformationally between the native and denatured states; (b)
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Searched by Mary Jane Ruhl x 22524

exposing the biol. active agent to a complexing perturbant to reversibly transform the biol. active

agent to the intermediate state and to form a transportable

supramol. complex; and (c) exposing the membrane or bilayer to the

supramol. complex, to transport the biol. active agent across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 Daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. active agent. In the present invention, the biol. active agent does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. active agent comprising steps (a) and (b) above is also provided as are oral delivery compns. Addnl., mimetics and methods for preparing mimetics are contemplated. Native gradient gels were run with 647 mg/mL of α -interferon, and increasing amts. (10-500 mg/mL) of perturbant (a mixture of L-Valine, L-Leucine, L-phenylalanine, L-lysine and L-arginine modified with benzenesulfonylchloride). As the amount of perturbant added was increased in each subsequent lane relative to a fixed concentration of α -interferon, the α -interferon migrated to a lower, rather than a higher, mol. weight This indicated that the α -interferon structure was changing, because if the structure was not changing, there would be a shift towards higher mol. weight as perturbant complexes with the active agent . Oral administration of above α -interferon and perturbant to rats at 500 $\mu q/kq$ showed significant blood level of α -interferon as compared with controls with no perturbant. REFERENCE COUNT: 734 THERE ARE 734 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L25 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:492070 HCAPLUS

FORMAT

DOCUMENT NUMBER:

133:109955

TITLE:

Amino acid derivatives and compositions therewith for

delivering active agents

INVENTOR(S):

Leone-Bay, Andrea; Ho, Koc-kan;

Sarubbi, Donald J.; Leipold, Harry R.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 44 pp., Cont.-in-part of PCT 9736480.

CODEN: USXXAM Patent

DOCUMENT TYPE:

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

| PATENT NO. | | | | | ND | DATE | | | APPLICATION NO. | | | | | DATE | | | |
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                                        JP 1998-535034
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                                                        A1 19980206
                                       WO 1998-US2619
                                                        W 19980206
     Carrier compds., especially amino acid derivs., and compns. therewith which are
AΒ
     useful in the delivery of active agents,
     e.g. peptides, mucopolysaccharides, carbohydrates, and lipids, are
     provided. Methods of administration and preparation are provided as well.
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L25 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

aqueous propylene glycol was prepared

intracolonic dosing composition containing parathyroid hormone 25 μ g/kg, 4-[4-(phenoxyacetyl)aminophenyl]butyric acid as carrier 100 mg/kg in 25%

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ACCESSION NUMBER:
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2000:475505 HCAPLUS

DOCUMENT NUMBER:

133:109945

TITLE:

Polymeric delivery agents comprising a

polymer conjugated to a modified amino acid or

derivative thereof

INVENTOR(S):

Milstein, Sam J.; Barantsevitch, Eugene N.;

Wang, Nai Fang; Liao, Jun; Smart, John E.; Conticello,

Richard D.; Ottenbrite, Raphael M.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA; Virginia

Commonwealth University PCT Int. Appl., 91 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: DATENT NO

| PA. | | | | KI | KIND DATE | | | | APPLICATION NO. | | | | | Ο. | DATE | | | |
|----------|--|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----------------|------------|-------------------|-------------------|-------------------|-------------------|--------------------------|-------------------|-------------------|-------------------|
| | | | | A2 200 A3 200 | | | | | | WO | 20 | 00-U | s476 | | 2000 | 0107 | | |
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| | RW: | ΚΖ, GH, | MD, GM, | RU, KE, | TJ, LS, | TM MW, | SD, | SL, | SZ | , 1 | ΓΖ, | UG, | ZW, | AT, | AM, BE, SE, | СН, | CY, | DE, |
| | 2358 1146 | CG, 463 | CI, | CM, | GA, A | GN, 2000 | GW, 0713 | ML, | MR | , 1 CA | NE, 200 | SN, 00-23 | TD, 3584 | TG 63 | 2000 | 0107 | БО, | Cr, |
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| JP NZ | BR 2000008590 JP 2002534363 NZ 512581 | | | T: A | 2 | 2002 2002 | | 1 | JP NZ | 200 | 00-59 00-51 | 9196: 1258: | 1 1 | 20000 |)107 | | | |
| US | ZA 2001005213 US 6627228 US 2003232085 | | | B. | 1 | 2003 | 0930 | | 1 | US | 200 | 01-88 | 3900! | 5 | 20010 20013 20030 | L009 | | |
| PRIORITY | | | | | | | | Ţ | US : WO : | 199 200 | 9 - 1 | L1521 JS476 | 73P 6 | P W | 19990 20000 20011 |)108)107 | | |

Polymeric delivery agents comprising a polymer conjugated to a ΑB modified amino acid or derivative thereof, delivery agent compds. and compns. comprising them which are useful in the delivery of active agents are provided. Poly(N-acryloxysuccinimide) was conjugated with N-(5-aminomethylsalicyloyl)-8-aminocaprylic acid (preparation given). Oral and intracolonic delivery composition comprising human growth hormone and above conjugate was administered to rats. At a dose of 200 mg/kg conjugate, the actual amount of delivery agent dosed was 20 mg/kg. With such a concentration of delivery agent complexed with polymer there was evidence of systemic delivery.

L25 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:117018 HCAPLUS

DOCUMENT NUMBER:

132:151567

TITLE:

Preparation of arylamidoalkylcarboxylic acids and

compositions for delivering active

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agents.
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INVENTOR(S):

Gschneidner, David; Leone-Bay, Andrea; Wang, Eric; Errigo, Lynn; Kraft, Kelly; Moye-Sherman, Destardi; Ho, Koc-Kan; Press, Jeffrey Bruce;

Wang, Nai Fang

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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KIND DATE APPLICATION NO. DATE
    PATENT NO.
                    ____
    _____
                                        -----
    WO 2000007979 A2 20000217
WO 2000007979 A3 20000518
                                      WO 1999-US17974 19990806
        W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
            CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP,
            KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
            MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
            TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
            RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
            ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
            CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
    CA 2339765
                   AA 20000217 CA 1999-2339765 19990806
                    A1 20000228
    AU 9954711
                                       AU 1999-54711
                    A2 20010530
                                      EP 1999-940967 19990806
    EP 1102742
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO
    BR 9912975
                   A
                          20010925
                                       BR 1999-12975
                                                        19990806
    TR 200100366
                    T2 20011121
                                       TR 2001-20010036619990806
    JP 2002522413
                    T2 20020723
                                       JP 2000-563614 19990806
    NZ 509410 A 20030829
ZA 2001000470 A 20010820
                                                      19990806
                                       NZ 1999-509410
                                       ZA 2001-470
                                                        20010117
PRIORITY APPLN. INFO.:
                                     US 1998-95778P P 19980807
                                     US 1998-98500P P 19980831
                                     US 1998-108366P P 19981113
                                     US 1999-119207P P 19990205
```

135 Title compds. are claimed. Thus, Me azeloyl chloride was added AB dropwise to 2-amino-p-cresol in aqueous NaOH at 0° to give a residue which was stirred with aqueous NaOH in THF to give 4-HO-5-MeC6H3NHCO(CH2)7CO2H. Title compds. at 100-300 mg/kg with parathyroid hormone at 25-200 µg orally or intracolonically in rats gave peak serum parathyroid hormone levels of 5-1459.71 pg/mL.

L25 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:98355 HCAPLUS

DOCUMENT NUMBER:

132:141984

TITLE:

Pulmonary delivery of active

agents

INVENTOR(S):

Milstein, Sam J.; Smart, John E.;

Sarubbi, Donald J.; Carozza, Monica; Flanders, Elizabeth; O'Toole, Doris; Leone-Bay, Andrea

WO 1999-US17974 W 19990806

; Gschneidner, David

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 47 pp.

CODEN: PIXXD2

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DOCUMENT TYPE:
LANGUAGE:
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Patent English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                   KIND DATE
                                        APPLICATION NO. DATE
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                                              _____
     WO 2000006184 A1 20000210 WO 1999-US16957 19990727
          W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
              DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE,
              KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
              MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
              TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,
              TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
              ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
              CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2338358 AA 20000210 CA 1999-2338358 19990727 CA 2338419 AA 20000210 CA 1999-2338419 19990727 WO 2000006534 A1 20000210 WO 1999-US17090 19990727
          W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
              DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE,
              KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
              MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
              TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,
              TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
              ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
              CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9953210 A1 20000221 AU 1999-53210
     AU 745290
                        B2 20020321
     AU 9953237
                       A1
                              20000221
                                             AU 1999-53237
                                                                19990727
     AU 751612
                       B2 20020822
     EP 1100522
                                         EP 1999-938806 19990727
                       A1 20010523
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO
                                           EP 1999-938842 19990727
                        A1 20010523
     EP 1100771
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO
     TR 200100922 T2 20010921
                                              TR 2001-20010092219990727
    TR 200100922 T2 20010921
BR 9912694 A 20020102
JP 2002521455 T2 20020716
NZ 509239 A 20021025
JP 2003517438 T2 20030527
NZ 509238 A 20030725
ZA 2001000227 A 20010807
ZA 2001000226 A 20010904
US 6642411 B1 20031104
US 6440929 B1 20020827
US 2003072740 A1 20030417
US 6693073 B2 20040217
US 2003225300 A1 20031204
BRITY APPLN. INFO.:
                                              BR 1999-12694 19990727
                                              JP 2000-562038
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                                             NZ 1999-509239
                                                                19990727
                                              JP 2000-562341
                                                                 19990727
                                             NZ 1999-509238
                                                                19990727
                                              ZA 2001-227
                                                                 20010109
                                             ZA 2001-226
                                                                 20010109
                                             US 2001-744862
                                                                20010419
                                           US 2001-744777
                                                                20010426
                                             US 2002-172582 20020614
                                              US 2003-600413
                                                                 20030620
PRIORITY APPLN. INFO.:
                                           US 1998-94267P P 19980727
                                           US 1998-104466P P 19981016
                                           WO 1999-US16957 W 19990727
                                           WO 1999-US17090 W 19990727
                                            US 2001-744862 A1 20010419
                                            US 2001-744777 A1 20010426
OTHER SOURCE(S):
                         MARPAT 132:141984
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Methods of administration of active agents via the

pulmonary route are provided. Thus, sodium 2-(4-(Nsalicyloyl)aminophenyl)propionate was prepared and 16 mg/kg this compound was mixed with 0.05 mg/kg porcine insulin and administered to rats by lung-spray-IT instillation. The AUC of the formulation wa higher than that without any carrier added. REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER:

L25 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN 1999:233788 HCAPLUS

DOCUMENT NUMBER:

130:287040

TITLE:

Delivery of biologically active

agents across cell membranes involving active

transport systems

INVENTOR(S):

Milstein, Sam J.; Leone-Bay, Andrea ; Sarubbi, Donald J.; Leipold, Harry Emisphere Technologies, Inc., USA

PATENT ASSIGNEE(S):

PCT Int. Appl., 164 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

| | PA! | | | | KIND DATE | | | | | | | | | | | | | |
|-------|------|--------------|-----|------|-----------|-----|------|------|-------|-------|--------|--------------|-----------|-----|----------------|------|------|------|
| | WO | 9916 | 427 | | A | 1 | 1999 | 0408 | | M | 0 19 | 98-U | S205 | | | | | |
| | | W: | | , | | | | , | | , | | , | | , | CN, | , | | , |
| | | | | | | | | | | | | | | | JP, MN, | | | |
| | | | | | | - | | | | | | | | | TM, | | | |
| | | | • | | | | | | | | | | | | RU, | | | 0117 |
| | | RW: | | | | | | | | | | | | | CY, | | | ES, |
| | | | | | | | | | | | | | | | ВJ, | | | |
| | | | | | GN, | | | | | | | | | | | | | |
| | | 6221 | | | | | | | | | | | | | | | | |
| | | 2304 | | | | | | | | | | | | | | | | |
| | | 9895 | | | | | | | | A | U 19 | 98-9. | 5136 | | 19980 | 0929 | | |
| | | 7356 1021 | | | | | | | | 177 | D 10 | 000 | 1 O E O ' | 7 | 1000 | 2020 | | |
| | LP | | | | | | | | | | | | | | NL, | | мС | DΨ |
| | | 11. | IE, | | C11, | DB, | DIV, | шо, | r IV, | GD, | GIV, | + + <i>I</i> | шт, | шо, | 1411, | JE, | rac, | ш, |
| | JР | 2001 | | | T | 2 | 2001 | 1009 | | J: | P 200 | 00-5 | 1356 | 5 | 19980 | 929 | | |
| | | 7710 | | | | | 2004 | 0311 | | | | | | | 20001 | 1214 | | |
| | | 7714 | | | | 2 | 2004 | 0325 | | | J 200 | | | | 2000 | | | |
| PRIOF | RITY | APP: | LN. | INFO | .: | | | | | | | | | | 19970 | | | |
| | | | | | | | | | | | | | | | 19920 | | | |
| | | | | | | | | | | | | | | | 19920 19930 | | | |
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| | | | | | | | | | | | | | | | 1993 | | | |
| | | | | | | | | | | | 993-: | | | | 1993 | | | |
| | | | | | | | | | | | | | 11 | A2 | 19940 | 302 | | |
| | | | | | | | | | Ţ | JS 1 | 994-2 | 23162 | 22 | A2 | 19940 |)422 | | |
| | | | | | | | | | Ţ | JS 1 | 994-2 | 23162 | 23 | В2 | 19940 | 1422 | | |
| | | | | | | | | | | | 994-1 | | | | 19940 | | | |
| | | | | | | | | | | | 994-1 | | | | 19940 | | | |
| | | | | | | | | | Ţ | JS 1: | 994-3 | 31640 | J4 | A2 | 19940 | 1930 | | |
| | | | | | | | | | | | | | | | 19941 19960 | | | |
| | | | | | | | | | , | JJ 1. | J 50~. | × 1 0 0 2 | L.E | Ľ | エラシひし | 1129 | | |

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US 1996-763183 A2 19961210
US 1997-820694 A2 19970318
AU 1998-62756 A3 19980206
WO 1998-US20548 W 19980929
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OTHER SOURCE(S): MARPAT 130:287040

Methods for transporting a biol. active agent across a cellular membrane or a lipid bilayer are disclosed. A first method includes the steps of: (a) providing a biol. active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. active agent to a complexing perturbant to reversibly transform the biol. active agent to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. active agent across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. active agent. In the present invention, the biol. active agent does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. active agent comprising steps (a) and (b) above is also provided as are oral delivery compns. Addnl., mimetics and methods for preparing mimetics are contemplated.

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:100747 HCAPLUS

DOCUMENT NUMBER:

130:144204

TITLE:

Modified amino acids as carriers for enhanced

delivery of active agents

INVENTOR(S):

Leone-Bay, Andrea; Ho, Koc-kan; Sarubbi, Donald J.; Milstein, Sam J.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 414,654.

CODEN: USXXAM

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|---|--|--|--|
| US 5866536 US 5650386 CN 1190893 JP 2003313157 US 6071510 AU 771024 AU 771434 PRIORITY APPLN. INFO.: | A A A A A2 A B2 B2 | 19990202 19970722 19980819 20031106 20000606 20040311 20040325 | US 1997-798033 US 1995-414654 CN 1996-192998 JP 2003-140962 US 1997-839094 AU 2000-72261 AU 2000-72260 US 1995-414654 | 19970206 19950331 19960401 19970423 20001214 20001214 |
| PRIORITI AFFEN. INFO. | | | US 1995-3111P P JP 1996-529751 A3 | 19950331 19950901 19960401 19980206 |

AB Carrier compds., compns., and dosage unit forms which are useful in the delivery of active agents are provided. The

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12/07/2004
     present invention provides compds. such as 10-salicyloylaminodecanoic acid
     (I) for delivery of at least one active agent
     , including peptides, mucopolysaccharides, carbohydrates, or lipids. I
     prepared from 8-aminocaprylic acid and 0-acetylsalicyloyl chloride was mixed
     with recombinant human growth hormone (rhGH) in a phosphate buffer solution
     The composition was orally administered to rats at I 200 mg/kg and rhGH 3 mg/kg
     and delivery was evaluated by an ELISA assay for rhGH; mean peak
     serum levels of rhGH was .apprx.60.92 ng/mL as compared to <0.1 ng/mL for
     control group received a composition without I.
REFERENCE COUNT:
                        13
                              THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L25 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:
                      1998:721669 HCAPLUS
DOCUMENT NUMBER:
                        130:7397
TITLE:
                        Compounds and compositions for delivering
                        active agents
INVENTOR(S):
                        Leone-Bay, Andrea; Gschneidner, David; Wang,
                        Eric; Sarubbi, Donald J.
PATENT ASSIGNEE(S):
                        Emisphere Technologies, Inc., USA
SOURCE:
                        PCT Int. Appl., 27 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
     PATENT NO. KIND DATE
                                    APPLICATION NO. DATE
     WO 9849135 A1 19981105 WO 1998-US7045 19980408
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR,
            KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
            UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
            FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
            CM, GA, GN, ML, MR, NE, SN, TD, TG
    US 5863944 A 19990126 US 1997-846254
                                                          19970430
    AU 9869590
                     A1 19981124
                                         AU 1998-69590
                                                          19980408
    AU 727068
                     B2 20001130
                     A1 20000216
    EP 979225
                                         EP 1998-915393 19980408
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
                                       JP 1998-547012 19980408
MX 1999-9632 19991020
    JP 2001524109
                      Т2
                           20011127
    MX 9909632
                     A 20000630
PRIORITY APPLN. INFO.:
                                      US 1997-846254 A 19970430
                                       WO 1998-US7045 W 19980408
    Carrier compds. and compns. which are useful in the delivery of
    active agents are provided, including
    N-2-(amino-5-fluorobenzoyl)-8-aminocaprylic acid, 4-(N-(5-fluoro-2-
    aminobenzoyl)-4-aminophenyl)butyric acid, and 8-(2-hydroxy-5-
    chloroanilinocarbonyl)octanoic acid. Methods of administration and preparation
    are provided as well.
REFERENCE COUNT:
                              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

L25 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:613457 HCAPLUS

DOCUMENT NUMBER: 129:250217 TITLE:

Oral **delivery** system comprising modified amino acids and biologically **active**

agents

INVENTOR(S):

Milstein, Sam J.; Barantsevitch, Evgueni N.

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 22 pp., Cont.-in-part of U.S. 5,447,728.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

20

PATENT INFORMATION:

PATENT ASSIGNEE(S):

| PATENT NO. | KIND DATE | APPLICATION NO. DATE |
|--|--|---|
| US 5443841 US 5451410 US 5578323 US 5447728 | A 19980922 A 19950822 A 19950919 A 19961126 A 19950905 | US 1992-920346 19920727 US 1993-51019 19930422 US 1993-76803 19930614 |
| W: AM, AT, | AU, BB, BG, BY, | CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, |
| RW: AT, BE, BF, BJ, | CF, CG, CI, CM, | FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, GA, GN |
| AU 771024 AU 771434 | B2 20040311 B2 20040325 | ZA 1994-8342 19941024 AU 2000-72261 20001214 AU 2000-72260 20001214 |
| PRIORITY APPLN. INFO | .: | US 1992-920346 A2 19920727 US 1993-51019 A2 19930422 |
| | | US 1993-76803 A2 19930614 US 1993-143571 B2 19931026 US 1993-168776 A2 19931216 WO 1994-US12333 W 19941024 |
| | | AU 1998-62756 A3 19980206 |

Modified amino acids and methods for their preparation and use as oral delivery systems for pharmaceutical agents are described. The modified amino acids are preparable by reacting single amino acids or mixts. of two or more kinds of amino acids with an amino modifying agent such as benzene sulfonyl chloride, benzoyl chloride, and hippuryl chloride. The modified amino acids may form encapsulating microspheres in the presence of the active agent under sphere-forming conditions. Alternatively, the modified amino acids may be used as a carrier by simply mixing the amino acids with the active agent. The preferred acylated amino acid carrier is salicyloyl-phenylalanine. The modified amino acids are particularly useful in delivering biol. active agents, e.g., desferrioxamine, insulin or cromolyn sodium, or other agents which are sensitive to the denaturing conditions of the gastrointestinal tract. Salicyloyl phenylalanine (I) was prepared from hydrogenolysis of salicyloyl phenylalanine benzyl ester (preparation given). Microspheres containing 1.5mg insulin/mL and 300 mg I/mL were prepared The sustained effect of the microspheres was shown in rats.

REFERENCE COUNT:

THERE ARE 343 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L25 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

343

ACCESSION NUMBER:

1998:548547 HCAPLUS

DOCUMENT NUMBER:

129:180147

TITLE:

Compounds and compositions for delivering

active agents

INVENTOR(S):

PATENT ASSIGNEE(S):

Leone-Bay, Andrea; et al. Emisphere Technologies, Inc., USA PCT Int. Appl., 147 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

| PATENT | INFORMATION: |
|--------|--------------|
|--------|--------------|

| PATENT NO. | KIND | DATE | | APPLICATION NO. DATE |
|---|--|--|---------------------------------|---|
| W: AL, ANDK, ER KZ, LC PL, P US, US | A1 1, AT, AU, 2, ES, FI, 2, LK, LR, 3, RO, RU, 5, US, US, | 19980813 AZ, BA, GB, GE, LS, LT, SD, SE, US, US, | BB, GW, LU, SG, US, | BG, BR, BY, CA, CH, CN, CU, CZ, DE, HU, ID, IL, IS, JP, KE, KG, KP, KR, LV, MD, MG, MK, MN, MW, MX, NO, NZ, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, UZ, VN, YU, PH TJ TM |
| ZW, AI RW: GH, GI FR, GI GA, GI US 5773647 US 5776888 US 5804688 US 5876710 US 5879681 US 5939381 US 5990166 US 6051561 US 6060513 US 6090958 US 6313088 US 6358504 AU 9862756 AU 738735 EP 1015008 R: AT, E JP 2001513080 NZ 337131 MX 9907290 | A, AZ, BY, A, KE, LS, B, GR, IE, N, ML, MR, A A A A A A A A A A B1 B1 A1 B2 A1 E, CH, DE I T2 A B2 B2 A1 | KG, KZ, MW, SD, IT, LU, NE, SN, 19980630 19980707 19980908 19990302 19990817 19991123 20000418 20000509 20000718 20011106 20020319 19980826 20010927 20000705, DK, ES, 20010828 20040311 20040325 20020829 20030103 20030225 | MD, SZ, MC, TD, FR, | NO, 13, 1M UG, ZW, AT, BE, CH, DE, DK, ES, FI, NL, PT, SE, BF, BJ, CF, CG, CI, CM, TG US 1997-796337 19970207 US 1997-796338 19970207 US 1997-796335 19970207 US 1997-796334 19970207 US 1997-796340 19970207 US 1997-797820 19970207 US 1997-797813 19970207 US 1997-797816 19970207 US 1997-797816 19970207 US 1997-797100 19970207 US 1997-797100 19970207 US 1997-796336 19970207 US 1997-796336 19970207 AU 1998-62756 19980206 EP 1998-905042 19980206 GB, GR, IT, LI, LU, NL, SE, MC, PT JP 1998-535034 19980206 NZ 1998-337131 19980206 MX 1999-7290 19990806 AU 2000-72261 20001214 AU 2000-72260 20001214 |
| | | | | US 1997-796340 A1 19970207 US 1997-796341 A1 19970207 US 1997-797100 A1 19970207 US 1997-797813 A1 19970207 |

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US 1997-797816
               A1 19970207
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US 1997-797820 A1 19970207
US 1996-17902P P 19960329
              A2 19970318
WO 1997-US5128
               A3 19980206
AU 1998-62756
              A3 19980206
EP 1999-117292
              W 19980206
WO 1998-US2619
               B1 20001219
US 2000-746548
                A1 20011031
US 2001-1731
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Carrier compds. and compns. which are useful in the delivery of active agents are provided. The carrier compound can be an amino acid derivative, and the active agent can be a peptide, mucopolysaccharide, carbohydrate, or lipid. Methods of administration, including oral administration, and preparation are provided as well. For example, an oral solution contained parathyroid hormone 100 μg , 4-[4-(phenoxyacetyl)aminophenyl]butyric acid (as carrier) 400 mg, and water 1L.

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS .7 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:542693 HCAPLUS

DOCUMENT NUMBER:

129:180125

TITLE:

Oral drug delivery compositions comprising modified amino acids and bioactive peptides

INVENTOR(S):

Sarubbi, Donald J.; Leone-Bay,

Andrea; Paton, Duncan R.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 18 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

| PATENT NO. | KIND DATE | | APPLICATION NO. | DATE | | | |
|---|---------------------------------------|---|--|--|-----|-----|----|
| CA 2160693 EP 696208 | A 1998081 AA 1994102 A1 1996021 | 7 4 | | 19940302 19940422 19940422 | | | |
| R: AT, BE, JP 08509474 EP 1025840 | T2 1996100 A2 2000080 | FR, 18 19 | GB, GR, IE, IT, LI JP 1994-523595 EP 2000-103527 | 13340424 | | PT, | SE |
| R: AT, BE, EP 1077070 | A2 2001022 | FR, 21 | GB, GR, IT, LI, LU EP 2000-118505 | , NL, SE, 19940422 | MC, | PT, | ΙE |
| AT 204467 ES 2163444 US 5643957 US 5714167 US 5958457 US 5766633 US 6099856 US 5955503 US 6100298 | CH, DE, DK, ES | FR, FR, 5)1 01 01 03 28 16 08 21 | US 1994-328932 US 1995-438644 US 1995-537888 US 1996-763183 US 1997-795833 US 1997-795837 | 19940422 19941025 19941025 19950510 19951023 19961210 19970206 | | PT, | IE |

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                                        US 2000-730156
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                                        AU 2000-72261
                        20040311
                    B2
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                                        US 2001-862013
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                    A1 20020502
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PRIORITY APPLN. INFO.:
                                                     A2 19920727
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                                                     A 19940302
                                      US 1994-205511
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                                                     A2 19940422
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                                      US 1994-315200
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                                      US 1994-316404
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                                      US 1994-328932
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                                      US 1994-335147
                                                     A3 19941025
                                      US 1994-335148
                                                     A1 19950510
                                      US 1995-438644
                                                     P 19960329
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                                                     A2 19961210
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                                                      A3 19980206
                                      AU 1998-62756
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                                                      A1 20010521
                                      US 2001-862063
                                                      A1 20020221
                                      US 2002-90012
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The present invention relates to an oral drug delivery system, and in particular to modified amino acid derivs. for use as a delivery system of sensitive agents such as bioactive peptides. The modified amino acid derivs. can form non-covalent mixts. with active biol. agents and in an alternate embodiment can releasably carry active agents. These mixts. are suitable for oral administration of biol. active agents to mammals.

Methods for the preparation of such amino acids are also disclosed.

REFERENCE COUNT: 341 THERE ARE 341 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L25 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN ACCESSION NUMBER: 1998:457247 HCAPLUS

DOCUMENT NUMBER:

129:113532

TITLE:

Compounds and compositions for delivering

active agents

INVENTOR(S):

Leone-Bay, Andrea; Wang, Eric; Sarubbi, Donald J.; Leipold, Harry Emisphere Technologies, Inc., USA

PATENT ASSIGNEE(S):

SOURCE:

U.S., 34 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

| PAT | ENT NO. | KIND DATE | | APPLICATION NO. DATE | |
|--|--|--|---|--|---|
| CA CA | DK, EF KZ, LC PL, PT US, US ZW, AN | A 199807 AA 199808 AA 199808 A1 199808 , AT, AU, AZ, E , ES, FI, GB, G , LK, LR, LS, I , RO, RU, SD, S , US, US, US, US, KG, E , KE, LS, MW, S | 07 113 113 8A, BB, GE, GW, LT, LU, GE, SG, US, US, | US 1997-796338 19970207 CA 1998-2319672 19980206 CA 1998-2319680 19980206 WO 1998-US2619 19980206 BG, BR, BY, CA, CH, CN, CU, CZ, DE HU, ID, IL, IS, JP, KE, KG, KP, KR LV, MD, MG, MK, MN, MW, MX, NO, NZ SI, SK, SL, TJ, TM, TR, TT, UA, UG US, US, US, US, US, UZ, VN, YU RU, TJ, TM UG, ZW, AT, BE, CH, DE, DK, ES, FI NL, PT, SE, BF, BJ, CF, CG, CI, CM | , |
| AU | GA, GN 9862756 | , ML, MR, NE, S A1 199808 | SN, TD, 326 | TG AU 1998-62756 19980206 | |
| ΕP | 738735 993831 | B2 200109 A2 200004 | 119 | EP 1999-117292 19980206 | |
| EP | 993831 R: AT, BI IE, FI | | ES, FR, | GB, GR, IT, LI, LU, NL, SE, MC, PT | ١, |
| EP | 1015000 | A1 200007 C, CH, DE, DK, E | 705 ES, FR, | EP 1998-905042 19980206 GB, GR, IT, LI, LU, NL, SE, MC, PT | · / |
| | 1093819 | A2 200104 | 514 | EP 2000-122704 19980206 | ۲, |
| JP JP NZ MX NZ NZ AU | R: AT, BI IE, F 2001131090 2001139494 2001513080 337131 9907290 507275 507276 771024 771434 Y APPLN. IN | A2 200109 A2 200109 T2 200109 A 200109 A 200111 A 200209 B2 20040 B2 20040 | 515 522 828 831 531 130 201 | GB, GR, IT, LI, LU, NL, SE, MC, PT JP 2000-311231 19980206 JP 1998-535034 19980206 NZ 1998-337131 19980206 MX 1999-7290 19990806 NZ 2000-507275 20001003 NZ 2000-507276 20001003 AU 2000-72261 20001214 AU 2000-72261 20001214 US 1997-796334 A 19970207 US 1997-796335 A 19970207 US 1997-796337 A 19970207 US 1997-796338 A 19970207 US 1997-796339 A 19970207 US 1997-796340 A 19970207 US 1997-796341 A 19970207 US 1997-796341 A 19970207 US 1997-797813 A 19970207 US 1997-797813 A 19970207 US 1997-797813 A 19970207 US 1997-797816 A 19970207 | , |

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US 1997-797820 A 19970207
AU 1998-62756 A3 19980206
CA 1998-2279331 A3 19980206
EP 1998-905042 A3 19980206
EP 1999-117292 A3 19980206
JP 1998-535034 A3 19980206
NZ 1998-337131 A1 19980206
WO 1998-US2619 W 19980206
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Carrier compds. and compns. which are useful in the delivery of AΒ

active agents are provided. Methods of administration

and preparation are provided as well. Standard methods of preparation are mentioned for

the 193 carrier compds. listed, which primarily are N-(fatty acid)

benzamide derivs. Examples are listed for the delivery of

parathyroid hormone, recombinant human growth hormone, interferon and the

evaluation of heparin in rats.

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 13 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:430107 HCAPLUS

DOCUMENT NUMBER:

129:113525

TITLE:

Compounds and compositions for delivering

active agents

INVENTOR(S):

Leone-Bay, Andrea; Wang, Eric; Sarubbi,

Donald J.; Leipold, Harry

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 35 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

| PATENT NO. | KIND DATE | APPLICATION NO. DATE |
|--|--|---|
| CA 2319672 | A 19980630 AA 19980813 AA 19980813 | US 1997-796337 19970207 CA 1998-2319672 19980206 CA 1998-2319680 19980206 |
| WO 9834632 | A1 19980813 | 3 WO 1998-US2619 19980206 |
| W: AL, AM, DK, EE, KZ, LC, PL, PT, US, US, | AT, AU, AZ, BA, ES, FI, GB, GE, LK, LR, LS, LT, RO, RU, SD, SE, | BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, VN, YU, |
| RW: GH, GM, FR, GB, GA, GN. | KE, LS, MW, SD, GR, IE, IT, LU, ML, MR, NE, SN, | SZ, UG, ZW, AT, BE, CH, DE, DK, ES, F1, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, TD, TG |
| AU 9862756 | A1 19980826 | 6 AU 1998-62756 19980206 |
| EP 993831 | A3 20010502 | 9 EP 1999-117292 19980206 2 |
| R: AT, BE, | CH, DE, DK, ES, | , FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, |
| R: AT, BE, | CH, DE, DK, ES, | 5 EP 1998-905042 19980206 , FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, |
| EP 1093819 | A2 20010425 | 5 EP 2000-122704 19980206 |

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A3 20030514
     EP 1093819
    R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
    JE, FI

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JP 2001139494 A2 20010522 JP 2000-311230 19980206

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MX 9907290 A 20000531 MX 1999-7290 19990806

NZ 507275 A 20011130 NZ 2000-507275 20001003

NZ 507276 A 20020201 NZ 2000-507276 20001003

AU 771024 B2 20040311 AU 2000-72261 20001214

AU 771434 B2 20040325 AU 2000-72260 20001214

RITY APPLN. INFO.:
              IE, FI
                                            US 1997-796334 A 19970207
PRIORITY APPLN. INFO.:
                                             US 1997-796335 A 19970207
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                                             US 1997-797817 A 19970207
                                             US 1997-797820 A 19970207
                                             AU 1998-62756 A3 19980206
                                             CA 1998-2279331 A3 19980206
                                             EP 1998-905042 A3 19980206
                                              EP 1999-117292 A3 19980206
                                              JP 1998-535034 A3 19980206
                                             NZ 1998-337131 A1 19980206
                                             WO 1998-US2619 W 19980206
     Carrier compds. and compns. therewith which are useful in the
AΒ
     delivery of active agents are provided.
     Methods of administration and preparation are provided as well. Standard
methods
     of preparation are mentioned for the 193 carrier compds. listed, which
     primarily are N-(fatty acid) benzamide derivs. Examples are listed for
     the delivery of parathyroid hormone, recombinant human growth
     hormone, interferon and the evaluation of heparin in rats.
                                   THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                             33
                                   RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L25 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:414634 HCAPLUS
DOCUMENT NUMBER:
                             129:72224
                            Oral drug delivery compositions and methods
TITLE:
                            Milstein, Sam J.; Barantsevitch, Evgueni N.;
INVENTOR(S):
                            Sarubbi, Donald J.; Leone-Bay, Andrea
                            ; Paton, Duncan R.
                            Emisphere Technologies, Inc., USA
PATENT ASSIGNEE(S):
                            U.S., 40 pp., Cont.-in-part of U.S. 5,451,410.
SOURCE:
                             CODEN: USXXAM
DOCUMENT TYPE:
                             Patent
                             English
LANGUAGE:
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:
                                                 APPLICATION NO. DATE
                     KIND DATE
      PATENT NO.
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A 19980616
A 19950919
A 19980811
B2 20040311
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                         А
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     US 5451410
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PRIORITY APPLN. INFO.:
                                                US 1994-205511 A2 19940302
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                                                AU 1998-62756 A3 19980206
OTHER SOURCE(S):
                            MARPAT 129:72224
     The present invention relates to an oral drug delivery system,
      and in particular to modified amino acids and modified amino acid derivs.
      for use as a delivery system of sensitive agents such as
     bioactive peptides. The modified amino acids and derivs. can form
      non-covalent mixts. with active biol. agents and in an alternate
      embodiment can releasably carry active agents.
     Modified amino acids can also form drug containing microspheres. These mixts.
      are suitable for oral administration of biol. active
      agents to animals. Methods for the preparation of such amino acids are
      also disclosed. In a test tube 568 mg acetyl phenylalanine aldehyde, 132
     mg carbomethoxyphenylalanylleucine, and 100 mg N-acetyl-Phe-Leu-Leu-Arg
      aldehyde were added to 2.9 mL of 15 % ethanol. The solution was stirred and
      NaOH was added to raise the pH to 7.2 and water was added to bring the
      total volume to 4 mL. Calcitonin 6 \mu g was added to the solution to obtain
      an oral solution
                                      THERE ARE 311 CITED REFERENCES AVAILABLE FOR
REFERENCE COUNT:
                              311
                                      THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
                                      FORMAT
L25 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
                              1998:402289 HCAPLUS
ACCESSION NUMBER:
                              129:86002
DOCUMENT NUMBER:
                              Active agent transport systems
TITLE:
                              Milstein, Sam J.; Barantsevitch, Evgueni;
INVENTOR(S):
                              Leone-Bay, Andrea; Wang, Nai Fang;
                              Sarubbi, Donald J.; Santiago, Noemi B.
                              Emisphere Technologies, Inc., USA
PATENT ASSIGNEE(S):
                              PCT Int. Appl., 134 pp.
SOURCE:
                              CODEN: PIXXD2
                              Patent
DOCUMENT TYPE:
                              English
LANGUAGE:
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:
      PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9825589 A1 19980618 WO 1997-US23545 19971209
          9825589

Al 19980618

WO 1997-US23545

19971209

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
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AU 771024 B2 20040311
AU 771434 B2 20040325
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PRIORITY APPLN. INFO.:

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WO 1997-US23545 W 19971209
AU 1998-62756 A3 19980206
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MARPAT 129:86002 OTHER SOURCE(S):

Methods for transporting a biol. active agent across a cellular membrane or a lipid bilayer. A first method includes the steps of: (a) providing a biol. active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. active agent to a complexing perturbant to reversibly transform the biol. active agent to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. active agent across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. active agent. In the present invention, the biol. active agent does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. active agent comprising steps (a) and (b) above is also provided as are oral delivery compns.

Addnl., mimetics and methods for preparing mimetics are contemplated. THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 1 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1997:672238 HCAPLUS

DOCUMENT NUMBER:

TITLE:

127:322800

Modified amino acids for drug delivery

INVENTOR(S):

Leone-Bay, Andrea

PATENT ASSIGNEE(S):

Emishphere Technologies, Inc., USA; Leone-Bay, Andrea

PCT Int. Appl., 64 pp. SOURCE: CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

| PATENT | NO. | | KI | ND | DATE | | | A. | PPLI | CATI | N NC | 0. | DATE | | | |
|---------|-----|-----|-----|-----|------|------|-----------------|-----|------|------|------|-----|------|------|-----|-----|
| | | | | | | | | _ | | | | | | | | |
| WO 9736 | 480 | | А | 1 | 1997 | 1009 | | W | o 19 | 97-U | S512 | 8 | 1997 | 0318 | | |
| W: | AL, | AM, | ΑT, | ΑU, | AZ, | ΒA, | BB, | BG, | BR, | BY, | CA, | CH, | CN, | CU, | CZ, | DE, |
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| | LK, | LR, | LS, | LT, | LU, | LV, | \mathtt{MD} , | MG, | MK, | MN, | MW, | MX, | NO, | NΖ, | PL, | PT, |
| | RO, | RU, | SD, | SE, | SG, | SI, | SK, | ТJ, | TM, | TR, | TT, | UA, | UG, | US, | UZ, | VN, |

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YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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                                        US 1996-17902 A1 19960329
PRIORITY APPLN. INFO.:
                                        US 1996-17902P P 19960329
                                        WO 1997-US5128 A2 19970318
                                        AU 1998-62756 A3 19980206
                         MARPAT 127:322800
OTHER SOURCE(S):
     Modified amino acid compds. useful in the delivery of
     active agents are provided. E.g., 2HOC6H4CONH(CH2)7CO2H
     was prepared from 8-aminocaprylic acid and 0-acetylsalicyloyl chloride.
     Also examples were give of a nol. of delivery agents enhancement
     of recombinant human growth hormone bioavailability administered s.c. in
L25 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:594748 HCAPLUS
                         127:248424
DOCUMENT NUMBER:
TITLE:
                         Preparation of small oligopeptides as agents for oral
                         drug delivery
                         Milstein, Sam J.
INVENTOR(S):
                         Emisphere Technologies, Inc., USA; Milstein, Sam J.
PATENT ASSIGNEE(S):
                         PCT Int. Appl., 143 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                 KIND DATE APPLICATION NO. DATE
     PATENT NO.
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     WO 9731938 A1 19970904 WO 1997-US4051 19970228
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             ML, MR, NE, SN, TD, TG
                 AA 19970904
                                          CA 1997-2247048 19970228
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         724209 A1 19970916 AU 1997-24209 19970228
883629 A1 19981216 EP 1997-919879 19970228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI
     AU 9724209
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                                        US 1996-12573P P 19960229
PRIORITY APPLN. INFO.:
                                        WO 1997-US4051 W 19970228
                        MARPAT 127:248424
OTHER SOURCE(S):
     The present invention relates to small oligopeptides pGlu(X)n and Pro(X)n
     (X = amino acid residue; n = 1 to about 10) and compns. prepared from them.
     Theses compns. comprising an oligopeptide, and an active
     agent are useful in the delivery of a cargo to a target,
     and particularly in the oral delivery of biol. or chemical
     active agents. Methods for the preparation and for the
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administration of such compns. are also disclosed. Thus, pyroglutamic acid

peptides H-pGlu-Glu(Phe-OH)-OH, H-pGlu-Glu(Phe-OH)-Phe-OH, and

H-pGlu-Glu-Phe-Tyr-OH, prepd, by standard solution coupling methods, showed heparin binding affinity parameters Kd = 1.42 + 10-4, 1.46 + 10-4, and 1.89 + 10-4, resp.

L25 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:527636 HCAPLUS

DOCUMENT NUMBER: 127:152958

TITLE: Modified amino acid carriers, their preparation, and

compositions containing them for delivering

active agents

Leone-Bay, Andrea; Paton, Duncan R.; INVENTOR(S):

Ho, Koc-Kan; DeMorin, Frenel

Emisphere Technologies, Inc., USA PATENT ASSIGNEE(S):

U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 231,622. SOURCE:

CODEN: USXXAM

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 30

| US 5643957 US 5451410 US 5792451 | A A A A | 19970513 19960502 | US 1994-335148 19941025 US 1993-51019 19930422 US 1994-205511 19940302 US 1994-231622 19940422 CA 1995-2203033 19951016 |
|---|---|---|---|
| CA 2203033 WO 9612473 W: AL, AM, A FI, GB, G | SE, HU | BB, BG, IS, JP, | WO 1995-US13527 19951016 BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, |
| RW: KE, MW, S | NL, PT, | | BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, |
| | A1 B2 | 19991021 | AU 1995-39633 19951016 EP 1995-937558 19951016 |
| R: AT, BE, C BR 9510168 HU 77759 JP 10507762 AT 249422 ES 2207655 US 5955503 US 6100298 NO 9701889 FI 9701776 US 2001003001 | CH, DE, A A2 T2 E T3 A A A A A1 B2 B2 A1 B2 | DK, ES, 19971014 19980728 19980728 20030915 20040601 19990921 20000808 19970623 19970425 20010607 20040311 20040325 20020829 20031216 20040408 | FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE BR 1995-10168 19951016 HU 1998-903 19951016 JP 1995-514062 19951016 AT 1995-937558 19951016 ES 1995-937558 19951016 US 1997-795833 19970206 US 1997-795837 19970206 NO 1997-1889 19970424 FI 1997-1776 19970425 US 2000-730156 20001205 AU 2000-72261 20001214 AU 2000-72260 20001214 US 2002-90012 20020221 US 1993-51019 A2 19930422 US 1994-205511 A2 19940302 US 1994-231622 A2 19940422 WO 1994-US4560 A2 19940422 |

WO 1995-US13527 W 19951016 US 1997-795837 A1 19970206 AU 1998-62756 A3 19980206 US 1999-346970 A1 19990702 US 2000-730156 A1 20001205 US 2002-90012 A1 20020221

OTHER SOURCE(S):

MARPAT 127:152958

GI

AB Modified amino acid compds. useful in the **delivery** of **active agents** (peptides, carbohydrates, antigens,

monoclonal antibodies, hormones, pesticides, etc.) are provided. Methods of administration and preparation are also provided. The effect of a composition

Ι

containing e.g. interferon- $\!\alpha 2$ and e.g. I (preparation given) on the serum interferon level was determined

L25 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:119253 HCAPLUS

DOCUMENT NUMBER: 126:135457

TITLE: Microspheres containing fragrances and flavorants

INVENTOR(S): Milstein, Sam J.

PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Milstein, Sam J.

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

KIND DATE APPLICATION NO. PATENT NO. _____ _____ WO 9640070 19961219 WO 1996-US10183 19960606 A1 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA 19981020 US 1995-484293 19950607 US 5824345 Α CA 2219035 AA 19961219 CA 1996-2219035 19960606 A1 19961230 AU 1996-62765 19960606 AU 9662765 19980401 EP 1996-921566 19960606 EP 831784 Α1 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 11507916 Т2 19990713 JP 1996-502232 19960606 US 1995-484293 A 19950607 PRIORITY APPLN. INFO .:

AB Compns. useful in the delivery of fragrances and flavorant

WO 1996-US10183 W 19960606

active agents, and particularly vaporous fragrances and flavorants, are provided. These compns. include a microsphere which includes: (a) the active agent; and (b) (1) a proteinoid, (2) a modified hydrolyzed vegetable protein wherein the protein is modified with an amino reactive agent, or (3) a combination thereof. Clove oil/proteinoid microspheres were prepared by combing a mixture of 0.1% clove oil in 10% soluble proteinoid (Glu-Asp-Tyr-Phe) with an equal volume of 1.7 N citric acid and gum to prepare microspheres of clove oil/proteinoid microspheres.

L25 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1997:87 HCAPLUS

DOCUMENT NUMBER:

126:31174

TITLE:

Preparation of modified amino acid compounds for

delivering active agents

INVENTOR(S):

Leone-Bay, Andrea; Ho, Koc-Kan; Sarubbi, Donald J.; Milstein, Sam J.

; Press, Jeffery Bruce

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA; Leone-Bay, Andrea; Ho, Koc-Kan; Sarubbi, Donald, J.; Milstein, Sam, J.;

Press, Jeffery, Bruce PCT Int. Appl., 86 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 30

| PA: | rent | NO. | | KI | ND | DATE | | | A | PPLI | CATI | ON N | 0. | DATE | | | |
|-----|--------------|------|-----|-----|--------|------|------|-----|-----|------|----------|------|-----|------|------|-----|-----|
| WO | 9630 | 036 | | | | | | | | | 96-U | S458 | 0 | 1996 | 0401 | | |
| | W: | AL, | AM, | AT, | ΑU, | AZ, | BB, | BG, | BR, | BY, | CA, | CH, | CN, | CZ, | DE, | DK, | EE, |
| | | ES, | FI, | GB, | GE, | HU, | IS, | JP, | KE, | KG, | ΚP, | KR, | KΖ, | LK, | LR, | LS, | LT, |
| | | LU, | LV, | MD, | MG, | MK, | MN, | MW, | MX, | NO, | NZ, | PL, | PT, | RO, | RU, | SD, | SE, |
| | | | SI | | | | | | | | | | | | | | |
| | RW: | KΕ, | LS, | MW, | SD, | SZ, | UG, | ΑT, | BE, | CH, | DE, | DK, | ES, | FΙ, | FR, | GB, | GR, |
| | | ΙE, | IT, | LU, | MC, | NL, | PT, | SE, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ | | |
| US | 5650 | 386 | | А | | 1997 | 0722 | | U | 5 19 | 95-4 | 1465 | 4 | 1995 | 0331 | | |
| CA | 2214 | 323 | | A. | A | 1996 | 1003 | | C | 19 | 96-2 | 2143 | 23 | 1996 | 0401 | | |
| ΑU | 9656 7122 | 629 | | Α | 1 | 1996 | 1016 | | Αſ | J 19 | 96-5 | 6629 | | 1996 | 0401 | | |
| ΑU | 7122 | 22 | | В | 2 | 1999 | 1104 | | | | | | | | | | |
| EΡ | 8176 | | | | | | | | | | | | | | | | |
| | R: | | | | | | | FR, | GB, | GR, | ΙT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | ΙE, | SI, | LT, | LV, | FI | | | | | | | | | | | |
| BR | 9604 | 880 | | A | | 1998 | 0519 | | Bl | ₹ 19 | 96-4 | 880 | | 1996 | 0401 | | |
| JΡ | 2002 | 5064 | 18 | T | 2 | 2002 | 0226 | | J | | | | | 1996 | | | |
| RU | 2203 | 268 | | C | 2 | 2003 | 0427 | | RI | | | | _ | 1996 | | | |
| JP | 2003 | 3131 | 5/ | A | 2 | 2003 | TTOP | | زل | | | | | 1996 | | | |
| US | 5965 | 121 | | A | | 1999 | 1012 | | U | | | | | | | | |
| US | 5989 6001 | 539 | | A | | 1999 | 1123 | | US | | | | | 1997 | | | |
| US | 6001 | 347 | | A | | 1999 | 1214 | | O: | | | | | 1997 | | | |
| | 9703 | | | | | | | | | | | | | 1997 | | | |
| | 9704 | | | | | 1997 | | | | | | | | 1997 | | | |
| | 2001 | | | | | 2001 | | | U | s 19 | 99-3 | 0550 | Ь | 1999 | USUS | | |
| | 6428 | 780 | | R | Z 1 | 2002 | | | F7. | 2 20 | 00.4 | 0005 | 0 | 2000 | 0000 | | |
| | 6346 | | | | | 2002 | | | | | | | | | | | |
| AU | 7710 | 24 | | В | 2 | 2004 | | | | | | | | 2000 | | | |
| | 7714 | | | | | | | | | | | | | | | | |
| | 2003 | | | | | 2003 | | | U; | 5 20 | 01-3 | 0420 | | 2001 | 1019 | | |
| US | 6623 | 131 | | В | _ | 2003 | 0923 | | | | | | | | | | |

| US 2003078302 US 6699467 | A1 B2 | 20030424 20040302 | | US 2002-14200 | 9 | 20020508 |
|-----------------------------|----------|----------------------|----|---------------|----|----------|
| US 2004110839 | A1 | 20040610 | | US 2003-62314 | 2 | 20030718 |
| PRIORITY APPLN. INFO.: | | | US | 1995-414654 | Α2 | 19950331 |
| | | | US | 1995-3111P | Ρ | 19950901 |
| | | | US | 1996-17902P | Ρ | 19960329 |
| | | | JP | 1996-529751 | ΑЗ | 19960401 |
| | | | WO | 1996-US4580 | W | 19960401 |
| | | | US | 1997-798031 | Α1 | 19970206 |
| | | | AU | 1998-62756 | AЗ | 19980206 |
| | | | US | 1999-305506 | Α1 | 19990505 |
| | | | US | 2000-499958 | Α1 | 20000208 |
| | | | US | 2001-38426 | Al | 20011019 |

OTHER SOURCE(S): MARPAT 126:31174

GΙ

$$HO_2C$$
 NH
 X
 II

AΒ Modified amino acid compds. [I (n = 0-3; m = 0-4; X = H, halo, OH, etc.), II (n = 0-3; X = 2-F, 3-MeO, 4-Me, etc.), etc.], useful in the delivery of active agents such as, e.g., human growth hormone, interferon, heparin, calcitonin, parathyroid hormone, were prepared Thus, reaction of 8-aminocaprylic acid with 0-acetylsalicyloyl chloride in the presence of 2M aqueous NaOH afforded 57% III which was mixed with recombinant growth hormone (rhGH) in a phosphate buffer solution at pH 7-8 and administered orally to rats at 25 mg/kg of carrier and at 1 mg/kg of rhGH. The mean peak serum level of compound III was 60.92 ng/mL as compared to < 10 ng/mL for control.

L25 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

1996:761910 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

126:37109

TITLE: Diamide-dicarboxylic acid microspheres

INVENTOR(S):

Milstein, Sam J.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA; Milstein, Sam, J.

SOURCE:

PCT Int. Appl., 78 pp. CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PA | TENT | NO. | | KI | ND | DATE | | | P | PPLI | CATI | ON N | ο. | DATE | | | |
|---------|-------|---------|------|-----|-----|-------|------|-----|------|-------|----------|-------|-----|------|------|-----|-----|
| WO | 9633 | 699 | | A | 1 | 1996 | 1031 | | M | 10 19 | 96-U | S650: | 2 | 1996 | 0429 | | |
| | W: | AL, | AM, | ΑT, | ΑU, | AZ, | BB, | ΒG, | BR, | BY, | CA, | CH, | CN, | CZ, | DE, | DK, | EE, |
| | | ES, | FI, | GB, | GE, | HU, | IS, | JP, | ΚE, | KG, | KΡ, | KR, | KΖ, | LK, | LR, | LS, | LT, |
| | | LU, | LV, | MD, | MG, | MK, | MN, | MW, | MX, | NO, | NΖ, | PL, | PT, | RO, | RU, | SD, | SE, |
| | | SG, | SI | | | | | | | | | | | | | | |
| | RW: | ΚE, | LS, | MW, | SD, | SZ, | UG, | ΑT, | BE, | CH, | DE, | DK, | ES, | FI, | FR, | GB, | GR, |
| | | ΙE, | ΙT, | LU, | MC, | NL, | PT, | SE, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN | |
| US | 5820 | 881 | | Α | | 1998. | 1013 | | Ü | S 19 | 95-4 | 3049 | 1 | 1995 | 0428 | | |
| CA | 2219 | 454 | | A | A | 1996 | 1031 | | C | A 19 | 96-2 | 2194 | 54 | 1996 | 0429 | | |
| AU | 9657 | 340 | | A | 1 | 1996 | 1118 | | P | U 19 | 96-5 | 7340 | | 1996 | 0429 | | |
| GB | 2314 | | | A | _ | | | | G | B 19 | 97-2. | 2756 | | 1996 | 0429 | | |
| GB | 2314 | 508 | | B: | 2 | 1999 | 0616 | | | | | | | | | | |
| PRIORIT | Y APP | LN. | INFO | .: | | | | | | 995- | | | | 1995 | | | |
| | | | | | | | | 1 | WO 1 | 996- | US 65 | 02 | | 1996 | 0429 | | |

AB Diamide-dicarboxylic acid microspheres are provided. The diamide-dicarboxylic acids may be combined with **active**

agent(s). The resultant composition may be in microsphere form. Also disclosed are methods for administering the microsphere and/or composition that includes the active agent. The microsphere, with or without active agent, may be prepared by (A) solubilizing, in a solvent, at least one diamide-dicarboxylic acid, to yield a first solution; and (B) contacting the first solution with a precipitator solution in which the diamide-carboxylic acid is insol. and optionally with an active agent. E.g., bis(No-amido-L-phenylalanine) malonate was prepared and used to prepare

L25 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

microspheres.

1996:494675 HCAPLUS

DOCUMENT NUMBER:

125:151187

TITLE:

Modified hydrolyzed vegetable protein microspheres and

methods for preparation and use

INVENTOR(S):

Milstein, Sam J.; Barantsevitch, Evgueni

PATENT ASSIGNEE(S): SOURCE:

Emisphere Technologies, Inc., USA

OURCE: U.S., 14 pp., Cont.-in-part of U.S. 5,401,516.

DOCUMENT TYPE:

Patent English

LANGUAGE:

Engl

FAMILY ACC. NUM. COUNT: 3

MENE INFORMACION.

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------|--------|----------|-----------------|----------|
| | | | | |
| US 5540939 | A | 19960730 | US 1994-233281 | 19940425 |
| US 5401516 | A | 19950328 | US 1993-51739 | 19930422 |
| PRIORITY APPLN. | INFO.: | | US 1992-995508 | 19921221 |
| | | | US 1993-51739 | 19930422 |

AB Modified hydrolyzed vegetable protein microspheres and methods for their

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preparation and use as oral delivery systems for pharmaceutical
agents, are described. A solution of soya proteins was treated with
benzenesulfonyl chloride. An aqueous solution containing heparin, gum acacia,
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and

citric acid was mixed with an aqueous solution containing heparin to give microspheres.

L25 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1996:434961 HCAPLUS

DOCUMENT NUMBER:

125:76328

TITLE:

Active agent transport systems using perturbants to convert active

agent to state between native and denatured

states

INVENTOR(S):

Milstein, Sam J.; Barantsevitch, Evgueni;

Leone-Bay, Andrea; Wang, Nai Fang; Sarubbi, Donald J.; Santiago, Noemi B.

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA PCT Int. Appl., 119 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

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KIND DATE
                                    APPLICATION NO. DATE
    PATENT NO.
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                                         ______
    _____
                    A1 19960502 WO 1995-US14598 19951024
    WO 9612475
        W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV,
            MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
            TJ, TM
        RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
            IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,
            NE, SN, TD, TG
                           19980203
                                        US 1994-328932
                                                          19941025
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                      Α
                                      CA 1995-2202300
                           19960502
    CA 2202300
                      AA
                                                          19951024
                                      AU 1996-41524
                           19960515
                                                          19951024
    AU 9641524
                      A1
                                                         19951024
                                        EP 1995-939863
                          19970702
    EP 781124
                     Α1
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
                    Т2
                           19980914 JP 1995-514159
                                                          19951024
    JP 10509433
                                         AU 2000-72261
                      B2
                           20040311
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    AU 771024
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                                         AU 2000-72260
                                                          20001214
    AU 771434
                      B2
                                      US 1994-328932 A 19941025
PRIORITY APPLN. INFO.:
                                      US 1992-898909
                                                       B2 19920615
                                      US 1992-920346
                                                      A2 19920727
                                      US 1993-51019
                                                      A2 19930422
                                      US 1993-76803
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                                      US 1993-143571
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                                                      A2 19931216
                                      US 1993-168776
                                                      A2 19940302
                                      US 1994-205511
                                                      A2 19940422
                                       US 1994-231622
                                                      A2 19940422
                                       US 1994-231623
                                       US 1994-315200
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                                       US 1994-316404
                                                      A2 19940930
                                       WO 1995-US14598 W 19951024
                                                      A3 19980206
                                       AU 1998-62756
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MARPAT 125:76328 OTHER SOURCE(S):

Methods are disclosed for transporting a biol. active agent across a cellular membrane or a lipid bilayer. A first method includes the steps of: (a) providing a biol. active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. active agent to a complexing perturbant to reversibly transform the biol. active agent to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. active agent across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant noncovalently bound or complexed with the biol. active agent. In the present invention, the biol. active agent does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. active agent comprising steps (a) and (b) above is also provided as are oral delivery compns. Addnl., mimetics and methods for preparing mimetics are contemplated. The methods and compns. of the invention facilitate the delivery of an active agent to a target, e.g. the delivery of a pharmaceutical through an adverse environment to a particular location in the body. The biol. active agent may be e.g. a carbohydrate, mucopolysaccharide, lipid, pesticide, or peptide, e.g. human or bovine growth hormone, an interferon, insulin, an antigen, a monoclonal antibody, cromolyn sodium, vancomycin, heparin, etc. The perturbant may be e.g. a proteinoid, carboxylic acid, or acylated amino acid or poly(amino acid). The perturbant may also be a pH-changing agent, an ionic strength-changing agent, or guanidine-HCl.

L25 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1996:425385 HCAPLUS

DOCUMENT NUMBER:

125:96071

TITLE:

Modified amino acids as absorption enhancers for

delivering active agents

INVENTOR(S):

Leone-Bay, Andrea; Paton, Duncan R.; Ho,

Kok-Kan; Demorin, Frenel

PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 57 pp.

CODEN: PIXXD2

20030910

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 30

В1

PATENT INFORMATION:

EP 783299

PATENT NO. KIND DATE APPLICATION NO. DATE ----WO 9612473 A1 19960502 WO 1995-US13527 19951016 W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG US 5643957 19970701 US 1994-335148 19941025 Α 19960515 AU 1995-39633 19951016 AU 9539633 A1 AU 711887 B2 19991021 EP 783299 A1 19970716 EP 1995-937558 19951016

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
                                     BR 1995-10168
     BR 9510168
                            19971014
                                                           19951016
                      A
     JP 10507762
                       Τ2
                            19980728
                                          JP 1995-514062
                                                            19951016
     AT 249422
                       E
                            20030915
                                          AT 1995-937558
                                                            19951016
     NO 9701889
                            19970623
                      Α
                                          NO 1997-1889
                                                            19970424
     FI 9701776
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                      Α
                                          FI 1997-1776
                                                            19970425
     AU 771024
                            20040311
                      В2
                                          AU 2000-72261
                                                            20001214
     AU 771434
                      В2
                            20040325
                                          AU 2000-72260
                                                            20001214
PRIORITY APPLN. INFO.:
                                        US 1994-335148 A 19941025
                                        US 1993-51019
                                                        A2 19930422
                                                        A2 19940302
                                        US 1994-205511
                                        US 1994-231622
                                                        A2 19940422
                                        WO 1995-US13527 W 19951016
                                        AU 1998-62756 A3 19980206
    Modified amino acid compds. as absorption enhancers are useful in the
     delivery of active agents. These compound are
     used as carriers to facilitate the delivery of a cargo to a
     target. Thus, 47.00 g acetylsalicyloyl chloride was added to a mixture of
     50.00 g 4-(4-aminophenyl)butyric acid in 300 mL of 2M aqueous sodium hydroxide
     and the reaction was stirred at 25° for 2 h, then it was acidified
     with aqueous HCl to obtain a precipitate which was separated and washed to
give 31.89 g
     4-(2-hydroxyphenylcarbonylamino)p-phenylbutanoic acid (I). I was mixed
     with interferon \alpha-2 (II) in Tris-HCl buffer pH = 7-8 and was orally
     administered to rats at a rate of 300 mg I/kg and 1000 \mu g II/kg. The
     mean peak serum level of II was 8213 as compared to 688 ng/mL for
     controls.
L25 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:
                         1996:417849 HCAPLUS
DOCUMENT NUMBER:
                         125:67703
TITLE:
                        Carbon-substituted diketopiperazine delivery
                        systems
INVENTOR(S):
                        Milstein, Sam J.
PATENT ASSIGNEE(S):
                        Emisphere Technologies, Inc., USA
SOURCE:
                        PCT Int. Appl., 25 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:
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| PAT | PATENT NO. KIND DA | | | | | DATE | | APPLICATION NO. | | | | 0. | DATE | | | | |
|-----|--------------------|------|-----|------|-----|------|------|-----------------|-----|------|---------------|-------|------|-------|------|-----|-----|
| WO | 9610 | 396 | | A. | 1 | 1996 | 0411 | | M |) 19 | 95 - U | S128 | 87 | 1995 | 0928 | | |
| | W: | | • | | | | | | | | | | | DK, | • | | • |
| | | , | GE, | | | | | , | • | | | | | LT, | , | • | |
| | | TM. | | MIN, | MA, | NO, | NΔ, | rь, | P1, | RO, | RU, | SD, | SE, | SG, | 51, | on, | 10, |
| | RW: | , | | SD, | SZ, | UG, | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙE, | IT, |
| | | LU, | MC, | NL, | PT, | SE, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | ML, | MR, | NE, |
| | | SN, | TD, | TG | | | | | | | | | | | | | |
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| ΑU | 7710 | 24 | | B | 2 . | 2004 | 0311 | | Α | J 20 | 00-72 | 2261 | | 2000 | 1214 | | |
| ΑU | 7714 | 34 | | B | 2 . | 2004 | 0325 | | Αl | J 20 | 00-72 | 2260 | | 20003 | 1214 | | |
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PRIORITY APPLN. INFO.:
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                                           WO 1995-US12887 W 19950928
                                          AU 1998-62756 A3 19980206
US 2001-929530 A1 20010813
                                           US 2002-125836 A1 20020419
OTHER SOURCE(S):
                          MARPAT 125:67703
     Compns. useful in the delivery of active
     agents are provided. These delivery compns. include (a)
     an active agent; and (b) a carrier of at least one
     mono-C-substituted or di-C-substituted diketopiperazine. E.g., the
     diketopiperazine derivative of glutamic acid was prepared and diketopiperazine
     derivs. microspheres were prepared cong. encapsulated salmon calcitonin.
L25 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:401663 HCAPLUS
DOCUMENT NUMBER:
                          125:67698
                          Diketopiperazine-based drug delivery systems
TITLE:
INVENTOR(S):
                          Milstein, Sam J.
PATENT ASSIGNEE(S):
                         Emisphere Technologies, Inc., USA
SOURCE:
                          PCT Int. Appl., 51 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                          English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:
     PATENT NO. KIND DATE
                                      APPLICATION NO. DATE
     WO 9609813 A1 19960404 WO 1995-US12888 19950928
         W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ,
             TM, TT
         RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
             SN, TD, TG
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                             19971202
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                                                               19940929
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     AU 9641293
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                             19991102
                                            US 1997-841101
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                                                               19970429
    AU 771024
                                           AU 2000-72261
AU 2000-72260
                             20040311
                                                               20001214
                       B2
     AU 771434
                             20040325
                                                               20001214
PRIORITY APPLN. INFO.:
                                          US 1994-315200 A 19940929
```

- AB Compns. useful in the delivery of active
 - agents are provided. These delivery compns. include:
 - (a) an active agent; and either (b)(1) a carrier of
 - (i) at least one amino acid and (ii) at least one diketopiperazine or (b)(2) at least one mono-N-substituted, di-N-substituted, or unsubstituted diketopiperazine. Methods for preparing these compns. and administering these compns. are also provided. Thus, 6 fasted rats were anesthetized. The rats were administered by oral gavage a calcitonin/L-Phe-(diketo-L-Asp)-L-Phe composition containing 1.5 μg of calcitonin/mL. Each rat was administered a dosage of 10 $\mu g/kg$. The amount of diketopiperazine in the dosage was 300 mg/kg. Blood samples were collected serially from the caudal artery, and serum calcium was determined. The carriers of the present invention facilitated the reduction of serum calcitonin and, therefore, the oral delivery of calcitonin.

WO 1995-US12888 W 19950928 AU 1998-62756 A3 19980206 L25 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1995:1000101 HCAPLUS

DOCUMENT NUMBER:

124:66617

TITLE:

Acids and acid salts and their use in delivery

systems

INVENTOR(S):

Leone-Bay, Andrea; Santiago, Noemi B. Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

30

PATENT INFORMATION:

PATENT ASSIGNEE(S):

| | PAT | CENT | NO. | | KI | ND | DATE | | | А | PPLI | CATI | ON NO | Э. | DATE | | | |
|------|------|-------|-----|-------|-----|--------|-------|------|-----|--------------|----------------|-------|-------|-----|-------|------|-----|-----|
| | WO | 9528 | 920 | | A: | 1 | 1995 | 1102 | | W | 0 19 | 95-U: | S511 |) | 1995 | 0421 | | |
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| | | | MG, | MN, | MX, | NO, | NΖ, | PL, | PT, | RO, | RU, | SD, | SE, | SG, | SI, | SK, | ТJ, | TM, |
| | | | TT, | UΑ | | | | | | | | | | | | | | |
| | | RW: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙE, | ΙT, | LU, | MC, | NL, | PT, | SE |
| | US | 5541 | 155 | | Α | | 1996 | 0730 | | U | S 19 | 94-23 | 31623 | 3 - | 19940 | 0422 | | |
| | ΑU | 9523 | 644 | | A. | 1 | 1995 | 1116 | | Α | U 19 | 95-23 | 3644 | | 19950 | 0421 | | |
| | ZA | 9503 | 246 | | Α | | 1996 | 0112 | | \mathbf{Z} | A 19 | 95-32 | 246 | | 19950 | 0421 | | |
| | ΑU | 7710 | 24 | | B | 2 | 20040 | 0311 | | Α | U 20 | 00-72 | 2261 | | 20003 | 1214 | | |
| | ΑU | 77143 | 34 | | B | 2 | 2004 | 0325 | | A | U 20 | 00-72 | 2260 | | 20001 | 1214 | | |
| PRIO | RITY | APP | LN. | INFO. | . : | | | | Ţ | JS 1 | 994- | 23162 | 23 | Α | 19940 | 0422 | | |
| | | | | | | | | | V | WO 1 | 995 - t | JS51: | 10 | W | 19950 | 0421 | | |
| | | | | | | | | | I | AU 1 | 998- | 62756 | 6 | АЗ | 19980 | 0206 | | |
| | | | | | | | | | | | | | | | | | | |

OTHER SOURCE(S):

MARPAT 124:66617

The present invention relates to a delivery system, and in particular to carboxylic acids for use as a delivery system, of sensitive agents such as bioactive peptides. The carboxylic acids and salts can form noncovalent mixts. with biol.-active agents. These mixts. are suitable for oral administration of biol. active agents to animals. An aqueous solution (pH 7.0-7.6) of cyclohexanepropionic acid sodium salt was mixed with

calcitonin to have a final carrier concentration 200 mg/mL and calcitonin concentration

5 μg/mL; the composition was orally administered to rats and serum Ca levels were monitored to show improved bioavailability as compared to the control which did not contain Na cyclohexanepropionate.

L25 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1995:992845 HCAPLUS

DOCUMENT NUMBER:

124:37744

TITLE:

Modified amino acids for drug delivery.

INVENTOR(S): PATENT ASSIGNEE(S): Leone-bay, Andrea; Wang, Nai Fang Emisphere Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| | | | | |
| WO 9528838 | A1 | 19951102 | WO 1995-US5112 | 19950421 |

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W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI,
             GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD,
             MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ,
             TM, TT
         RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
             SN, TD, TG
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                                            US 1994-231622
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                       AΑ
                            19951102
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                       A1
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     EP 758843
                       Α1
                            19970226
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         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
     JP 09512279
                       T2
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     AU 771024
                       B2
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                       В2
                            20040325
                                                             20001214
PRIORITY APPLN. INFO.:
                                        US 1994-231622 A 19940422
                                        WO 1995-US5112
                                                         W 19950421
                                        AU 1998-62756
                                                         A3 19980206
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OTHER SOURCE(S): MARPAT 124:37744

Th invention relates to an oral delivery system, and in particular to modified amino acids or peptides, for delivery sensitive agents such as bioactive peptides. The modified amino acids or peptides can form no-covalent mixts. or microspheres with active biol. agents. These mixts. or microspheres are suitable for oral administration of biol. active agents to animals. Methods for the preparation of such amino acids and peptides, for example N-cyclohexanoyl-Ltyrosine, are disclosed.

L25 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1995:951479 HCAPLUS

DOCUMENT NUMBER:

124:15498

TITLE:

Modified amino acids for encapsulating active

agents

INVENTOR(S): PATENT ASSIGNEE(S): Milstein, Sam J.; Barantsetvich, Evgueni N.

Emisphere Technologies, Inc., USA

U.S., 9 pp.

SOURCE:

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English 30

FAMILY ACC. NUM. COUNT:

| PATENT NO. KI | ND DATE | APPLICATION NO. | DATE |
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| US 5447728 A | 19950905 | US 1993-168776 | 19931216 |
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| EP 1025840 A | 2 20000809 | EP 2000-103527 | 19940422 |
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| R: AT, BE, CH, | DE, DK, ES, FR, | GB, GR, IT, LI, LU | , NL, SE, MC, PT, IE |
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| R: AT, BE, CH, | DE, DK, ES, FR, | GB, GR, IT, LI, LU, | , NL, SE, MC, PT, IE |

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| AU 771024 | B2 | 20040311 | | 2000-73015 | O | 20001205 |
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| US 2002052422 | A1 | 20020502 | IIS | 2001-86206 | 3 | 20010521 |
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| US 2004062773 | A1 | 20040401 | | 2002 23323 | | 20020923 |
| US 2004068013 | A1 | 20040408 | | 2003-67790 | | 20031001 |
| PRIORITY APPLN. INFO.: | | | | 92-898909 | | 19920615 |
| | | | | 02-920346 | | 19920727 |
| | | | | 3-51019 | | 19930422 |
| | | | | 3-76803 | | 19930614 |
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| | | | | 3-168776 | | 19931216 |
| | | | | 4-205511 | A | 19940302 |
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| | | | US 199 | 6-763183 | Α2 | 19961210 |
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| | | | | 9-420200 | | 19991018 |
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| | | | | | | 20010521 |
| | , | Ī | US 200 | 2-90012 | Α1 | 20020221 |
| | | | | | | |

Modified amino acids and methods for their preparation and use as oral AΒ delivery systems for pharmaceutical agents are described. The modified amino acids are preparable by reacting single amino acid or mixts. of two or more kinds of amino acids with an amino modifying agent such as benzenesulfonyl chloride, benzoyl chloride, and hippuryl chloride. The modified amino acids form encapsulating microspheres in the presence of the active agent under sphere-forming conditions. Alternatively, the modified amino acids may be used as a carrier by simply mixing the amino acids with the active agent. The modified amino acids are particularly useful in delivering peptides, e.g. insulin or calmodulin, or other agents which are sensitive to the denaturing conditions of the gastrointestinal tract. A mixture of 16 amino acids was treated with benzenesulfonyl chloride and the product dissolved in distilled water was mixed with a salmon calcitonin solution at 40° to obtain a microsphere suspension, suitable for oral administration.

L25 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1995:846860 HCAPLUS

DOCUMENT NUMBER:

123:266168

TITLE:

Modified amino acids for oral delivery of

sensitive bioactive agents

INVENTOR(S):

Milstein, Sam J.; Barantsevitch, Evgueni

PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA

SOURCE:

U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 51,019.

CODEN: USXXAM

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 30

| PATENT NO. | | APPLICATION NO. | DATE |
|---|--|---|---|
| US 5447728 US 5443841 US 5451410 US 5578323 CA 2174961 WO 9511690 W: AM, AT, HU, JP, | A 19950905 A 19950822 A 19950919 A 19961126 AA 19950504 A1 19950504 AU, BB, BG, BY, KE, KG, KP, KR, | US 1993-168776 US 1992-920346 US 1993-51019 US 1993-76803 CA 1994-2174961 WO 1994-US12333 CA, CH, CN, CZ, DE, DK, | 19930422 19930614 19941024 19941024 ES, FI, GB, GE, |
| BF, BJ, AU 9480936 ZA 9408342 EP 726771 | CF, CG, CI, CM, A1 19950522 | GA, GN AU 1994-80936 ZA 1994-8342 EP 1994-932077 | 19941024 |
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| AT 212186 ES 2171471 US 5714167 US 5811127 US 6099856 | E 20020215 T3 20020916 A 19980203 A 19980922 A 20000808 | FR, GB, GR, IT, LI, LU, AT 1994-932077 ES 1994-328932 US 1996-635921 US 1996-763183 US 1997-939939 US 1997-940056 US 1997-941616 | 19941024 19941024 19941025 19960424 19961210 |

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PRIORITY APPLN. INFO.:
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                                     AU 1998-62756 A3 19980206
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Modified amino acids and methods for their preparation and use as oral delivery systems for pharmaceutical agents are described. The modified amino acids are preparable by reacting single amino acids or mixts. of two or more kinds of amino acids with an amino modifying agent such as benzene sulfonyl chloride, benzoyl chloride, and hippuryl chloride. The modified amino acids form encapsulating microspheres in the presence of the active agent under sphere-forming conditions. Alternatively, the modified amino acids may be used as a carrier by simply mixing the amino acids with the active agent. The modified amino acids are particularly useful in delivering peptides or other agents which are sensitive to the denaturing conditions of the gastrointestinal tract. For example, an oral composition containing desferrioxamine (I) and salicyloyl phenylalanine was administered to monkeys to evaluate iron clearance efficacy; oral administration of I in the absence of the modified amino acid induced little clearance of iron, in contrast, I prepared with the amino acid carrier induced a rapid secretion of iron in both urine and feces.

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L25 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
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ACCESSION NUMBER:

1995:532343 HCAPLUS

DOCUMENT NUMBER:

122:274108

TITLE:

Modified hydrolyzed vegetable protein microspheres and

methods for preparation and use thereof

Milstein, Sam J.; Barantsevitch, Evqueni N.

INVENTOR(S): PATENT ASSIGNEE(S):

Emisphere Technologies, Inc., USA

SOURCE:

U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 995,508,

abandoned. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

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WO 9414420 A1 19940707 WO 1993-US12700 19931221
             W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, LV, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, UZ, VN RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
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                         A 19941109 CN 1993-119951 19931221
A1 19951004 EP 1994-906480 19931221
       CN 1094611
       EP 674507
             R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
       JP 08507043 T2 19960730 JP 1993-515498 19931221
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
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                                        19940824
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                         AA 19941027 CA 1994-2160692 19940422
A1 19941108 AU 1994-66685 19940422
A1 19960214 EP 1994-915419 19940422
       CA 2160692
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            R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
       JP 08509231 T2 19961001 JP 1994-523596 19940422 US 5540939 A 19960730 US 1994-233281 19940425 US 5972387 A 19991026 US 1994-342900 19941121
PRIORITY APPLN. INFO.:
                                                         US 1992-995508 19921221
US 1993-51739 19930422
                                                          WO 1993-US12700 19931221
WO 1994-US4561 19940422
      Modified hydrolyzed vegetable protein microspheres and methods for their
      preparation and use as oral delivery systems for pharmaceutical
      agents are described. For example, an acid-hydrolyzed liquid soybean
      protein solution was reduced and extracted with methanol; the obtained soybean
      protein was dissolved in an aqueous solution of KOH while heating. Thereafter,
      benzenesulfonyl chloride was added to the mixture to obtain modified
      proteins, which were used to manufacture insulin-encapsulated microspheres.
      The insulin microspheres were orally administered to rats and the results
      showed that encapsulated insulin had a greater biol. effect, in contrast
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L25 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
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ACCESSION NUMBER:

to unencapsulated insulin.

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DOCUMENT NUMBER:

120:226961

TITLE:

Proteinoid carriers and methods for preparation and

use thereof

INVENTOR(S):

Milstein, Sam J.; Kantor, Martin L. Emisphere Technologies, Inc., USA PCT Int. Appl., 104 pp.

PATENT ASSIGNEE(S): SOURCE:

CODEN: PIXXD2

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PRIORITY APPLN. INFO.:
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     Proteinoid carriers are prepared from peptides having 2-20 amino acids and a
AΒ
    mol. weight of 250-2400 daltons as a delivery system for a biol.
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AB Proteinoid carriers are prepared from peptides having 2-20 amino acids and a mol. weight of 250-2400 daltons as a **delivery** system for a biol. **active agent**, a fragrance, a cosmetic agent, etc. The proteinoids are soluble within selected pH ranges in the gastrointestinal tract and display enhanced stability towards photolysis or decomposition over time. For example, a proteinoid carrier encapsulating murine IgG monoclonal antibody was prepared having final concentration of 50 mg/mL proteinoid

prepared from a reaction mixture containing Glu, Asp, Tyr, and Phe at 1:1:1:1

ratio, the antibody 0.7 mg/mL, and gum arabic 0.5% in 0.85 N citric acid.